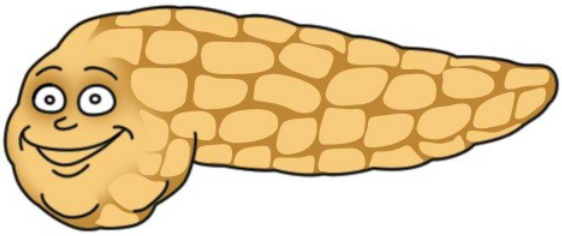

HEALTHY PANCREAS, HEALTHY YOU

Part I

STRUCTURE, FUNCTION AND DISORDERS OF THE PANCREAS

For patients and health practitioners

Peter Melamed, PhD

Felix Melamed, LAc, MSTCM, CHt

E-book version of **HEALTHY PANCREAS, HEALTHY YOU** consist of three interrelated parts:

Disclaimer. The purpose of this book is to educate. These statements have not been evaluated by the Food and Drug Administration. The information contained in this book is not intended to diagnose, treat, cure or prevent any disease. The authors and Biotherapy Alternative Medicine Clinic shall have neither liability nor responsibility to any person or entity with respect to any loss, damage, or injury caused or alleged to be caused directly or indirectly by the information contained in this book.

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http://www.biotherapy-clinic.com/

E-mail: info@biotherapy-clinic.com

As a pampered pet or as a lurked panther, it built its head in the bend of duodenum. It sprawled its delicate body on the aorta and aorta lullabies it by rhythmic pulsation movements. It carelessly put its slightly curved tail in the spleens gate. Yes, it is as a beautiful predator, which, when disease strikes, can unexpectedly cause irreparable injury.

This is your pancreas, is beautiful as the angel of heaven, but can be as daemon deceptive and evil. Your pancreas is a hard worker, an organ of many talents and tasks.

Save it, help it, heal it.

Authors

CONTENTS

Part I

STRUCTURE, FUNCTION AND DISORDERS OF THE PANCREAS

d. How Does the Sphincter of Oddi Dysfunction Occur?

e. Symptoms of Sphincter of Oddi Dysfunction

f. Who is affected by SOD?

Chapter 9-Pancreatitis, Acute Pancreatitis

a. History of Pancreatitis:

b. Frequency and Epidemiology of Pancreatitis:

Chapter 10-Chronic Pancreatitis

a. History of Chronic Pancreatitis

b. Chronic Pancreatitis Definition

c. Who is at Risk for Chronic Pancreatitis?

d. Classifications of Chronic Pancreatitis

e. Signs and Symptoms of Chronic Pancreatitis

i. Pain

ii. Exocrine Pancreatic Deficiency

iii. Endocrine Pancreatic Deficiency/Diabetes

f. Chronic Pancreatitis Complications

g. What are the Consequences of Chronic Pancreatitis?

Chapter 11-Alcoholic Pancreatitis

a. Males vs. Females

b. Research

c. Harmful Effects of Alcohol on the Pancreas

d. Alcohol and Pancreatic Enzymes

e. Alcohol and Candida

f. Alcohol and Pancreatitis

g. Alcohol and Acidity

h. Alcohol and Toxicity

Chapter15-Intestinal Dysbiosis: Candida-yeast Overgrowth, Small Intestine Bacterial Overgrowth (SIBO)

a. What Is Candida?

b. What is Dysbiosis?

c. How Does Dysbiosis Effect Pancreatic Health?

d. Typical Chronic Candidiasis Patient Profile

e. Candida-yeast overgrowth can totally disrupt digestion in many ways

I. Toxic Yeast Metabolites Directly Influence on Pancreatic Function and Digestive Enzymes

II. Causing chronic body acidity

III. Promoting Leaky Gut Syndrome

IV. Decreasing Immune System Function

V. Promoting Small Intestine Bacterial Overgrowth (SIBO)

f. Control of Microorganisms in the GI tract

g. How Does Small Intestinal Bacterial Overgrowth (SIBO) Occur?

h. Candidiasis

i. Why Are Dysbiosis and Candida-Yeast Overgrowth Prevalent Conditions in the Modern World?

j. What Do Dysbiosis and Candida-Yeast Overgrowth Cause in the Human Organism?

k. Undetected Candidiasis

l. Small Intestine Bacterial Overgrowth (SIBO)

m. The Harmful Effect of Dysbiosis on Exocrine Pancreatic Function and Digestion

n. Dysbiosis triggers low exocrine pancreatic function

i. Link Between Dysbiosis, the Decreased Activity of Pancreatic Digestive Enzymes Inside the Small Intestine and Subsequent Indigestion

ii. Deficiency of the Vital Nutrients in Dysbiosis

iii. Dysbiosis and Body Acidification

iv. Candida, Alcohol and Acetaldehyde - Toxic Substances for Pancreatic Cells

v. Candida and Chronic Pancreatic Inflammation

a. Who Is At Risk of Mineral Deficiency?

Chapter 25-Supplementation with Vitamins

Chapter 26-Supplementation with Essential Amino Acids and Essential Fatty Acids

Chapter 27-Alkalizing Diet for Pancreatic Health: In Balance with Nature

Chapter 28-Chronic Metabolic Acidosis and the Modern Western Diet

a. Acute and Chronic Conditions Accompanying Metabolic Acidosis
b. Modern Food and Metabolic Acidosis
c. Alkalizing Ability of Various Foods
d. The Pre-Agricultural Diet of Our Ancestors Was Alkaline-Formed

Chapter 29-Water: Best Friend of the Pancreas

Chapter 30-Dietary Recommendations for *Acidic Pancreas and Bile* Stage

a. What Should I Eat?
b. What Foods Should Be Avoided or Eaten in Very Low Amounts?
c. Food Combinations

Chapter 31-Dietary Recommendations for *Pancreatic Deficiency* Stage

a. Separation Diet
b. Diet for Candida-yeast overgrowth and/or Small Intestine Bacterial Overgrowth (SIBO)
c. Fructose Malabsorption
d. Low FODMAP Diet
e. Another Hidden Enemy for Digestive Health – Lectin
f. Multiple Foods Sensitivity, Intolerance and Food Allergies
g. Elimination Diet
h. Diet for Gastro-Esophageal Reflux Disease (GERD)
i. Diet for Metabolic Syndrome, Overweight Issues & Diabetes
j. Diet for Fatty Liver and Pancreas
k. Diet for Gallbladder Diseases

Chapter 36-Massage, Point Massage, Chiropractic Manipulations, and Abdominal Manual Therapy

a. Abdominal and Body Self-Massage

b. Abdominal Manual Therapy

Chapter 37-Therapeutic Exercises

a. Recommendation for Performing Exercises

b. Exercises Have Tremendous Impact on Organs and Systems

c. Cleansing the Entire Gastrointestinal Tract by Drinking KVHMW and Exercises

d. Role of Physical Activity and Special Healing Exercises in the Pancreatic Disorders

Chapter 38-The Mind /Body Connection and Pancreas

a. Hypnosis for Digestive Health

b. Hypnosis for Chronic Abdominal Pain

c. Hypnosis for Depending on Alcohol and Painkillers

Chapter 39-Whole Body Cleansing through the Restoration of Friendly Intestinal Flora and Colon Hydrotherapy

a. Possible Benefits of Colon Hydrotherapy

b. Inner Toxicity from Medical Standpoints

c. Pancreas and Inner Toxicity

d. Program That Decreases Inner Toxicity and Promotes Pancreatic Function

Chapter 40-Biotherapy Outpatient Program for Alcohol Cessation

a. Healing the Addicted Person and Addicted Brain Chemistry

1). Elimination of Alcohol and Products of its Metabolism – Detox/Detoxification

2). Brain Chemistry Normalization

3). Acid-Alkaline Balance Normalization

4). Subconscious Programming

5). Healing of Alcohol Related Health Problems

Chapter 41-A Non-drug Approach for Abdominal Pain

About the Authors

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FOREWORD

The pancreas is a forgotten organ in the human body.

By the way, where is your pancreas located? Very few people point their fingers in the right place. It is almost one of the unknown organs in the gastrointestinal tract. Very few are familiar with normal pancreatic function too. The popular pancreatic interests are centered mostly with diabetes and pancreatic cancer.

This book is about the pancreas. Writing this kind of book causes the serious dilemma of how to make the reading of this book useful and easy to understand for people without a medical background and, from another hand, making it practical for the medical professionals, which don't need popularization, but are interested in scientific dates and clinical details?

1st chapter section

The authors have their own writing style. Every beginning of a chapter will have a section ***"for individuals lacking a medical background"*** devoid of getting into the jungle of heavy medical and chemical terminology. This section of the book is for average individuals without deep medical knowledge but with common sense and willingness to learn more. In this case, simple words, charts, analogies, and pictures will be used.

It is difficult to find a person that does not have digestion problems. The digestive system, or gastrointestinal tract, includes hollow tube organs, such as the mouth, throat, esophagus, stomach, small and large intestines as well as solid glands such as the salivary glands, liver, and pancreas.

The pancreas is a vital organ for our body. People can survive without the stomach, small intestine, and colon but not without the pancreas. Life depends on this small gland, deeply hidden inside the abdomen cavity. The pancreas is an organ with dual tasks. Most individuals are only aware about the role of the pancreas in sugar metabolism, and that pancreas produces insulin, the vital hormone to prevent diabetes.

The second function of the pancreas is producing digestive enzymes - powerful proteins that split food we eat into particles small enough to travel through the intestinal wall so that we can digest and assimilate this food.

Ask anyone around and almost everyone has some sort of unpleasant GI symptoms: gas, abdominal distention, belching, heartburn, abdominal cramps, pains, nausea/vomiting, diarrhea/constipation, and so on.

What many people do not realize is that the function of many organs and systems and the whole body's health, strongly depend upon the health of our digestive system.

Our health and life depends upon the quality and amount of food we eat and how we can digest this food, assimilate this food, eliminate waste. The pancreas is a key player in the digestive team. This book focuses about the close relationship between the liver, gallbladder, pancreas, and intestines. Normally, these organs work as orchestra, but in sick conditions, they are bickering foes.

From this book, you will learn about the connection of the endocrine (hormonal) and exocrine (producing and releasing digestive enzymes) functions of the pancreas.

- How to improve the function of the pancreatic gland, as a whole organ?
- How to increase production and activity of digestive pancreatic enzymes?
- How to help the pancreas to heal and postpone severe complications after the first attack?
- How to help sick and weak pancreas without drugs and knives?

Here, readers will find the answers to these very important questions.

Most human diseases depend on two big problems:

1. The deficiency of vital substances in the body such as water, proteins, minerals, trace elements, vitamins and so on. As your car without gasoline stops moving, so will the deficiency of the vital nutrients stop the organs from performing their proper tasks

2. Toxicity (chemical or biological): Toxicity literally kills the cells and harmfully influences the body's metabolism causing inflammation, pain, cancer development and so on

These two factors are directly related to pancreatic health. Besides that, this book will try to explain how the whole body acidity – metabolic acidosis destroys the pancreas and proper work of pancreatic enzymes and pancreatic hormones.

Millions of Americans suffer from a variety of gastrointestinal disorders including abdominal pain, stomach discomfort, cramps, gas, bloating, heartburn, cravings, malnutrition, alteration in bowel habits, foul-smelling stool, etc. Many of these sufferers have pancreatic deficiency and do not realize it.

Those suffering from this problem can eat a healthy diet, but the body will not properly utilize the food's nutrients. Their organisms are literally starving. Some people can be overweight, but their body can have severe malnutrition. Without the proper amount, and good quality of pancreatic digestive enzymes, even the "healthiest" diet in the world will not make you healthy, good looking and young.

Without the proper function of the pancreas, which produces the right amount of high quality digestive, pancreatic enzymes, people cannot properly digest food; therefore, they suffer also from a deficiency of essential minerals, trace elements, and vitamins. This deficiency leads to serious disturbances of the gastrointestinal tract and the entire organism.

Millions of people are continually tired, develop chronic diseases, and age prematurely. In the worst case scenario, they develop pancreatic cancer.

People can suffer from a hidden pancreatic deficiency and do not even know that a lack of the pancreatic digestive enzymes can also increase inflammation, body's pain, and a lack of energy, hindering the body's ability to heal the wounds and traumas.

The popular health books and websites focus on the liver, colon, heart and stomach but not on the pancreas. On the other hand, there is not much medical literature concerning pancreatic health either. Various specialists have different opinions focusing on different aspects of the pancreatic health.

This sounds a lot like the story about six blind men who were asked to determine what an elephant looked like by feeling different parts of the elephant's body. The blind men guessed that the elephant looked either like a pillar, rope, tree branch, hand fan, wall or solid pipe from feeling the elephant's leg, tail, trunk, ear, belly and tusk (in that order). All the blind men were correct, but this was far from the real picture obviously.

In this book, you will find personal viewpoints from the authors on digestive (pancreatic) problems, which are confirmed by common sense, years of the authors' personal clinical experiences but also scientific information from many respectful researchers and medical doctors.

If you have health problems, you will find many recommendations in this book. Do not use them as medical advice. Try to find knowledgeable medical providers to work with. Belief, willingness, patience, and self-discipline are required for this job.

2nd chapter section

The rest of each chapter is provided ***for individuals with medical backgrounds*** wishing to know more and, certainly, for medical professionals. Reading this material requires some medical background.

Today, researchers and medical practitioners look at the pancreas and make different points of view on cause, development, and possible treatment of its disorders and diseases according to their own specialty.

Having medical experience in acute intensive care, outpatient clinic and private practice in digestive disorders' allows the authors sharing of thoughts about pancreatic health.

Some topics about pancreatic health in this book are new and will sound strange to some.

To convince conservative, but interested in this topic persons, more than 300 referrals from respectful and reputable medical books, textbooks, magazines, articles, and websites are referenced. These referrals are scientific and clinical works regarding pancreatic function, health, disorders of the pancreas and their treatment of respectful and well known professors, researchers, medical doctors and health practitioners from the USA, Canada, North and South America, Europe, Asia, Russia, etc.

Medically speaking, the pancreas by itself is also in a strange situation. Disorders of the exocrine function of this organ are the priority of the gastroenterologists, but other specialists treat pancreatic endocrine diseases such as diabetes.

Let's take, for example, chronic pancreatitis. Even authorities in pancreatic diseases do not have a consensus what is the main reason for developing this serious disease.

In all medical schools' textbooks of gastroenterology, for example, Yamada T *et al*, Sleisenger & Fordtran's, etc., it can be seen that the clinical presentation of chronic pancreatitis starts from steatorrhea, malabsorption, diabetes, pain and weight loss. This condition in the medical literature is called "pancreatic insufficiency". Sorry to say, it is not pancreatic insufficiency; this is real pancreatic failure similar to kidney, liver, heart and lung failure.

Clinical description of chronic pancreatitis begins from the final stage of this disease, when only 10% functional capacity is left, and the treatment approach is very limited. This is a medical paradox.

From the first attack of pancreatitis to pancreatic failure takes about 8 -15 years. Therefore, the focus has to be done in this time to prevent pancreatic failure, which is called chronic pancreatitis now. Even for brilliant specialists with virtuous technique and sophisticated equipment it is not an easy task to help patients when the pancreatic tissue and 90% functionality is gone.

Successful treatment of pancreatic diseases nowadays is generally difficult and requires many different approaches. Exocrine pancreatic disorders are more common than formerly believed both in diabetic and nondiabetic people. For instance, autopsy studies indicate pancreatic involvement in 13% of a “normal” population. Some clinical studies find the relation between functional digestive diseases and low pancreatic function. In almost all chronic diseases of the gastrointestinal tract, exocrine pancreatic function is diminished.

87,000 cases of pancreatitis annually occur in the USA. This is only the tip of the iceberg of digestive (pancreatic) diseases. Acute and chronic pancreatitis are diseases on the rise.

The diagnosis of chronic pancreatitis can be challenging since laboratory studies and imaging procedures may be normal, especially in the beginning of this process. Most attacks of pancreatitis are mild and go undiagnosed.

Some authorities in the pancreatic field consider that 8% of diabetes mellitus cases are caused by chronic pancreatitis. On the other hand, a large number of diabetics suffer from digestive problems, as well.

According to the statistics, the epidemic of obesity leads to a rise in epidemic proportions of nonalcoholic fatty liver disease (fatty liver). There is growing evidence that the fatty liver combines with the fatty pancreas with lowering of both their functions.

More than 25 million people in the United States suffer from liver, bile duct, or gallbladder diseases, according to the American Liver Foundation. No question that in many of these cases there is close pancreatic involvement.

The authors’ viewpoint that the pandemic of digestive (pancreatic) disorders is strongly interrelated with the pandemics of metabolic acidosis and dysbiosis will be attempted to be proven in this book.

Medical providers can help their patients by focusing on early stages of the pancreatic disorders. The authors propose that the practical clinical classification of the exocrine pancreatic deficiency stages be the following: functional, structural, and irreversible. For each of these stages, the reader will find healing programs and recommendations.

It is time for medical professionals to reassess established protocols dealing with pancreatic health. Medical practitioners are used to looking at the pancreas as an “accessory” digestive

gland. Yet, here it is considered that the pancreas is one of the body's essential organs. Moreover, it is believed that all gastrointestinal health critically depends upon the proper functioning of this vital organ.

Basic scientific and clinical evidence currently encourages a fresh holistic look at the development of pancreatic disorders, particularly a comprehensive look at the pancreas as a whole and vital organ.

In the minds of the authors, here are the most salient points:

> Almost all problems of the GI tract are closely related with the proper functioning of the pancreas. Therefore, a clinical diagnosis of a gastrointestinal disorder *de facto* includes pancreatic disorders.

> The pancreas is the main organ of the entire digestive system. It is vital for the pancreas to have strong and healthy relationships and connections to its "neighbors" and "co-workers" such as the liver, gallbladder, stomach, duodenum, small and large intestines.

> Today, the medical view on digestive disorders narrowly focuses on the "hollow" organs such as the stomach, small and large intestines without any attention on the "solid" digestive glands such as the pancreas and liver. It is known that without proper quality and quantity of pancreatic juice and bile, the normal digestive process in hollow chambers could not occur.

> Furthermore, it is important to look at the close relationship between exocrine and endocrine functions of the pancreas when assessing pancreatic disorders. Both pancreatitis and diabetes are diseases of the pancreas, and they have many similarities in point of causes, development, symptoms, course, complications, and treatment.

> Pancreatic disorders develop relatively slowly, therefore, medical professionals need to be more sensitive and focus on the first silent signs and symptoms at the beginning of the illness.

> The treatment of pancreatitis at the final stage of the disease is very difficult; preventive measures and treatment at the early stages of these diseases are more likely to stop or reverse the progression of the disease and to postpone pancreatic failure.

> Normal pancreatic function is vitally dependent upon maintaining homeostasis of the body. Metabolic acidosis and a deficiency of proteins, vitamins, minerals, trace elements, and bicarbonates have a serious and negative impact on pancreatic function, digestion and entire health.

> For healing purposes, it is essential to focus on the patients' lifestyle and diet and their possible impact on the development of pancreatic disorders.

> It is difficult to overestimate the positive or negative impact of food on digestive (pancreatic) disorders. Therefore, the patient must be taught the proper customized healing diet and then must adhere to the dietary recommendations.

>Digestive (pancreatic) disorders must be observed with an outlook on the regulation of the pancreas by digestive hormones, as well as the nervous and endocrine systems

> Positive changes of harmful environmental, toxic, parasitic, and dysbiotic factors are necessary for the prevention and treatment of digestive (pancreatic) disorders.

This book is an attempt for a fresh and deep holistic look into the pancreas, its structure, and function as a vital organ for whole body. This book focuses on the many ways to improve the functions of the pancreas by using non-drug, non-surgery approaches. These rational approaches have been used for hundreds of years by medical doctors and health professionals all over the globe for millions of their patients to improve the digestive (pancreatic) health.

The authors have used many of these methods in their practice for decades with positive results. Some of these holistic, alternative and complementary approaches for healing and avoiding pancreatic disorders are absolutely unknown by the American public and medical professionals, for example, using healing mineral water and a medical diet for pancreatic aliments.

Because the pancreas is a very complicated essential organ with many puzzles and mysteries, prevention and treatment of pancreatic disorders are very difficult problems and require many disciplinary approaches.

The authors consider that there is only one medicine to help people prevent and treat the diseases, but that implementation can be different. Successful treatment of pancreatic diseases requires a team approach and practitioners of complementary or alternative medicine can be very good players in this process, especially in the early stages.

The authors emphatically believe that healing approaches described in this book can improve the quality of life and life span of sufferers of pancreatic diseases.

The medical credo of the authors: ***"The treatment of disease must be less dangerous than the disease by itself!"***

The authors hope that this book will be useful to many different health professionals: medical doctors, naturopathic physicians, RNs, chiropractors, herbalists, acupuncturists, nutritionists, and colon hydro therapists and, most importantly, for the hundreds and thousands of sufferers with the digestive (pancreatic diseases).

Evidence based clinical and scientific practice has been shown in this book:

A healthy pancreas means a healthy organism

Authors

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Part I

STRUCTURE, FUNCTION AND DISORDERS

OF THE PANCREAS

Chapter 1-Pancreas. Explanation of Pancreatic Structure and Function

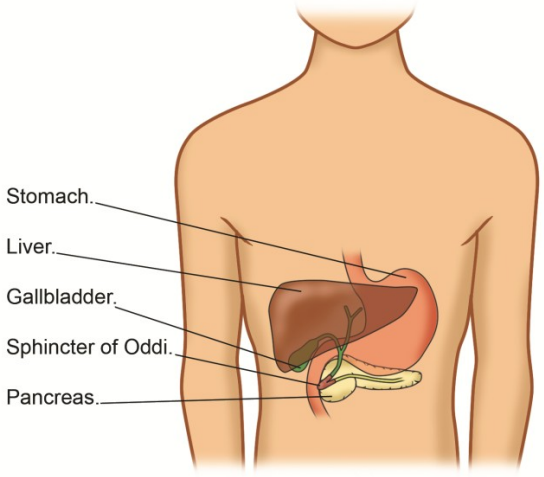
For individuals lacking a medical background

Many people don't know a lot about their pancreas. If average individuals would be asked where their pancreas is located or function of the pancreas, many of them would scratch their head. You might hear the vague answer "It is somewhere inside the stomach", "pancreas causes diabetes", "pancreatic cancer is an awful disease" and so on.

The pancreas does not have as much attention as other inner organs. If you will "google" the pancreas or other organs of our body such as the heart, brain, liver or kidney, you will see the amount of web sites about the pancreas is 5 to 50 times less often than the other organs. This book has a lot of information and it will help to know more about this vital organ in the human body.

The Greek name "pancreas", meaning "all flesh" or "all meat", is descriptive of the protein composition of this powerful organ.

By the Way, Where is the Pancreas Located?



The pancreas is called the "hidden organ" because it is located deep in the abdomen behind and below the stomach. Because of the hidden position, it is difficult to touch this organ through the abdominal wall. The pancreas is a fish-shaped organ about 6 to 8 inches long (15 cm) located in the middle and back portion of the abdomen. The right portion of the pancreas, called the head, is the largest portion, lying in the curve of the duodenum, the beginning of the small intestine. The smallest portion of the pancreas, the tail, ends near the spleen. The pancreas is connected to the first part of the small intestine, the duodenum, and to the gallbladder duct.

What Does the Pancreas Do?

Pancreas is a vital organ in our body. It is vital because our body cannot live without it. If people lose the pancreas due to trauma, inflammation or surgery, their lives shall be miserable and they will need serious life support.

The pancreas, or pancreatic gland, is unusual among the body's glands. This is the gland with double duties. On one hand, it produces hormones such as insulin and glucagon, which are critical in regulating blood sugar levels. Our cells cannot obtain energy for proper function without those hormones.

On the other hand, the pancreas produces very important digestive enzymes. Without them our body cannot digest vital nutrients from food such as proteins, fats, carbohydrates, vitamins, minerals, etc. People can eat “very healthy”, but if the pancreas does not produce the right amount and right quality of digestive enzymes, their body and eventually their cells will starve and breakdown.

Its cells manufacture a lot of pancreatic juice fulfilled with digestive enzymes. Released pancreatic juice is picked up by the small pancreatic ducts and carried into a large, main duct of the pancreas. This duct of the pancreas joins with the common bile duct and together they empty into the duodenum through the Sphincter of Oddi. The Sphincter of Oddi is a muscle valve between merged pancreatic and bile ducts and the duodenum. It is sort of a gait to help the moving of the mixture of the pancreatic juice and bile into the small intestine as a “one way road”.

How is the Secretion of Pancreatic Juices Controlled?

It is a very complicated process and is regulated mostly by the nervous system and hormones.

The central nervous system, which is stimulated by the organs of sense such as the tongue, eyes, ears, nose and skin, sends the message to whole digestive organs including the pancreas: “Be prepare, food is coming soon”. Everything is important here: mood, fear, enjoyable food, distraction from the eating process, hurrying up, environment, etc. It is known that the body does what the mind says.

Another way the secretion of pancreatic juices is regulated is via the autonomic nervous system. This system works involuntary. We can sleep, but our body works: the heart pumps the blood, lungs breathe, food is digested and so on. The vagus and sympathetic nerves transmit signals from the brain to the stomach, pancreas, gallbladder, and other digestive organs for a proper teamwork of their functions.

The digestive process also regulates the secretion of pancreatic juices by special blood messengers known as digestive hormones. The greatest role in regulation and stimulation of the pancreas appears to be exerted by the hormones CCK (cholecystokinin) and secretin. These digestive hormones are produced by cells in the wall of the duodenum. CCK stimulates the release of large quantities of pancreatic enzymes, whereas secretin causes water and bicarbonate secretion. As soon as this occurs, the enzymes secreted by the pancreatic cells are flushed out of the pancreas, through the pancreatic duct into the duodenum.

For individuals with a medical background

Some Historical Standpoints:

The existence of the pancreas first was mentioned in the Talmud (writings on Jewish law and traditions) between 200 BC and 200 AD, where it was described as the "finger of the liver."

The ancient anatomist regarded the pancreas as unusual, given that it had no cartilage or bone present, and Rufus of Ephesus (c.100 AD) named this organ pancreas (Greek *pan*: all, and *kreas*: flesh or meat).[17]

The following famous anatomists identified and described pancreatic anatomy and physiology:

- Johann Wirsung of Italy identified the pancreatic duct in 1642

- Abraham Vater of Germany described the papilla of Vater, a small nipple-like bulge, commonly called the Ampulla, where the pancreatic and common bile ducts enter the duodenum in 1720

- Giovanni Santorini of Italy described the pancreatic accessory duct in 1724

- Claude Bernard of France suggested the pancreas might have a role in digestion in 1850

- Rugerio Oddi of Italy described the muscle sphincter – valve bearing his name in 1869. This valve controls the flow of digestive juices (bile and pancreatic juice) through the ampulla of Vater into the first part of the small intestine (duodenum)

- Reginald Fitz of the USA discovered pancreatitis as a disease in 1889

- Paul Langerhans of Germany established the pancreas' connection with diabetes in 1890

- Eugene Opie of the USA implicated the gallstones as a cause of pancreatitis in 1901

- Frederick Banting and Charles Best of Canada were able to make a pancreatic extract, which had anti diabetic characteristics in 1921. Therefore, insulin was developed

From the 1970s until present, endoscopic retrograde cholangiopancreatography (ERCP), angiography, computed tomography (CT) scans, ultrasound, and magnetic resonance imaging clearly identified the pancreas opposing the long hiding of this gland. In recent years many noninvasive tests were developed to study pancreatic functions, as well.

Anatomy and Physiology

The pancreas is also called the pancreatic gland. A gland is an organ that produces substances that pass either into the main blood circulation (called an endocrine function), or pass into another organ and usually may connect to the outside (called an exocrine function). **Endo** is the Greek word for “inside”, “within”. **Exo** means "outside" in Greek. The thyroid, adrenal glands, ovaries or testicles are examples of endocrine glands because they produce special substances –

hormones that go into the blood as chemical messengers, which transport a signal from one cell to another or one organ to a different organ mostly for regulation of the human metabolism or specific body's actions.

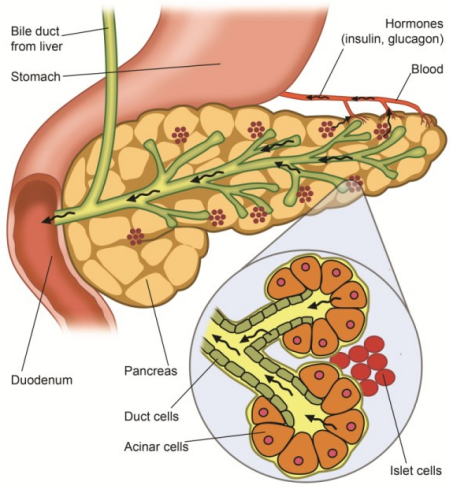
Typical exocrine glands include sweat glands, salivary glands, breasts/mammary glands, prostate, etc. Exocrine glands usually secrete their products into the ducts, which have the connection to the outside.

Between the glands, the pancreas is unique because it does double duty as producer of the digestive enzymes, which go into the pancreatic duct and intestines, and from another hand, the pancreas produces insulin that travels into the blood and is so vital in blood sugar control.

Structure (anatomy) and function (physiology) of the pancreas and its endocrine and exocrine tasks are interrelated. To understand the development of pancreatic disorders one needs to look at the pancreas as a whole organ that works as very important player of both the digestive and hormonal systems.

The pancreas lies beneath the stomach in the midline of the back of the abdomen, closely associated with the liver, stomach, and duodenum, the first part of the small intestine. (See the picture).

Endocrine cells are the cells that secrete products into the bloodstream. The endocrine portion of the pancreas, called the Islets of Langerhans, contains cells that produce hormones: insulin, glucagon and somatostatin. Insulin lowers blood sugar, while glucagon raises blood sugar.



Somatostatin has varying effects on the nervous system, pancreas, digestive system, and the pituitary gland. The endocrine portion constitutes roughly 2% of the total mass of the pancreas, the rest being the exocrine part.

The exocrine pancreas is a complex gland that contains many units that produce pancreatic juice. These exocrine cells produce enzymes that aid in digestion, including proteases to break down proteins, lipases to break down fats and amylase to break down carbohydrates. The cells in the pancreas that produce digestive enzymes are called acini or acinar cells (from Latin *acinus*, "grape"), so named because the cells aggregate to form bundles that resemble a cluster of grapes.

Acini are arranged into circular glands and are attached to small ducts. The ducts eventually combine to form the large pancreatic duct that carries pancreatic juice - a mixture of minerals, sodium bicarbonate and digestive enzymes, into the lumen of the duodenum – the first part of small intestine.

Pancreatic ducts are thin tubes that come together like the veins of a leaf. The pancreatic duct merges with the common bile duct at the Ampulla of Vater. The pancreatic juice mixes with the bile and is forced through a muscular valve called the Sphincter of Oddi into the duodenum. Enzymes are produced within the pancreatic acinar cells, packaged into storage vesicles called zymogens, and then released via the pancreatic ductal cells into the pancreatic duct, where they are secreted into the small intestine to begin the digestive process.

Interesting facts at a glance:

The pancreas lies beneath the stomach in the midline of the back of the abdomen. It is closely associated with the liver, stomach, and the duodenum

The pancreas is a unique gland because it is the only gland that has double function: exocrine and endocrine

The pancreas produces digestive enzymes, which go through the pancreatic duct into the intestines; this is an exocrine function

The pancreas also produces and releases into the blood the hormone insulin, which is so important in the control of blood sugar; this is an endocrine function

Pancreatic exocrine cells = acinar cells

Pancreatic endocrine cells = the Islets of Langerhans

Cells with exocrine function release an alkaline fluid containing sodium bicarbonate, electrolytes, and enzymes into the pancreatic duct, than into the small intestine

Pancreatic "juice" aids in breakdown and digestion of food in the small intestine

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Chapter 2-Composition of Pancreatic Juice

For individuals lacking a medical background

The pancreas is a hard worker. It normally produces almost 60-85 oz of a clear, colorless, alkaline fluid with a pH of 8.3. This is pancreatic juice, which consists of highly important ingredients for digestion such as water, minerals, proteins, bicarbonates, and enzymes. It is known that pancreatic enzymes need an alkaline environment for proper functioning. This is why, the pancreas produces a lot of bicarbonates – alkaline materials for neutralization of acidity

of partially digested food, which travels from the stomach into the duodenum. This partially digested food is called chyme and is usually extremely acidic.

For individuals with a medical background

The pancreas secretes pancreatic juice that is transported by the pancreatic duct into the duodenum. Pancreatic juice contains water, minerals, trace elements, bicarbonate, and many digestive enzymes such as trypsin, lipase, and amylase.

The pancreas produces 1.5 – 2.2 liters (8 – 12 cups) of clear, isotonic with plasma, alkaline pancreatic juice with relatively large amounts of protein fluid. Pancreatic juice has a pH of 8.0 – 8.3, thus, is much more alkaline than arterial blood which has a pH of 7.4.

Mainly the epithelial cells of small ducts leading from acini secrete two very important components of pancreatic juice, water and bicarbonate ions. The bicarbonate ion concentration can rise to as high as 145 mEq/liter, a value approximately five times that of bicarbonate ions in the plasma. Obviously, this provides a large quantity of alkaline ions in the pancreatic juice, which serve to neutralize the acid in the partly digested food (chyme) emptied into the duodenum from the stomach. It is important that

1 c.c. of pancreatic juice is capable of practically neutralizing an equal quantity 10c.c. of normal hydrochloric acid.[61]

Ball EG *et al.* (1941) from Harvard Medical School in Boston performed an acute experiment involving bicarbonate formed from radioactive carbon. They found that by injecting this bicarbonate into the bloodstream, its concentration in the pancreas increased by as much as 4-5 times in comparison to the serum. It was concluded that the plasma bicarbonate is the chief source of the pancreatic juice bicarbonate.[115]

Bicarbonate in pancreatic juice highly depends on the amount of bicarbonate in blood. According to the scientific literature and their own research, Scratcherd T, Case RM. (1973), considered that bicarbonate in pancreatic juice is critically dependent upon the amount of bicarbonate in the blood. Therefore, the higher capacity of “bicarbonate buffer” in the blood makes it easier for the pancreatic cells to take the bicarbonate from the blood in order to make the pancreatic juice strongly alkaline.[188]

Experiments by Norwegian scientists Raeder M., Mo A., Aune S. published in *Acta Physiologica Scandinavica* (2008), show a proportional relationship between HCO-3 pancreatic secretion and plasma pH. Pancreatic HCO-3 secretion increased to 196% plus – minus 10% of control during alkalosis and fell to 41% plus – minus 4% of control during acidosis. Plasma H+ ion concentration, therefore, seems to determine the rate of pancreatic HCO-3 secretion.[173]

All of the enzymes produced in the pancreas in normal conditions are active only in the small intestine. Pancreatic juice is released into the duodenum through a duct and valve in response to acidic chyme from the stomach entering the small intestine. The pH in the duodenum is 7.5 (alkaline) due to the sodium bicarbonate that is found in pancreatic juice and bile to neutralize stomach acid.

The important inorganic parts of the pancreatic juice are cations such as sodium, potassium, calcium, magnesium, zinc, and anions such as bicarbonate, chloride, and phosphate.

As mentioned earlier, the principal function of the exocrine pancreas is to make food-digesting enzymes, which mostly are proteins. The pancreas, comprising only 0.1% of total body weight, has 13 times the protein-producing capacity of the liver and the reticuloendothelial system combined, which make up 4% of total body weight.[11]

Digestive enzymes are produced in the acinar cells of the pancreatic gland that contain the machinery for protein production. Enzymes are produced within the pancreatic acinar cells, packaged into storage vesicles called zymogens, and then released via the pancreatic ductal cells into the pancreatic duct, where they are secreted into the small intestine to begin the digestive process.

Scientists consider that the type of food may influence the quality and quantity of enzymes. For example, eating a large amount of carbohydrates can increase activity of amylase and eating a lot of proteins can increase the production of protease that subsequently digests proteins.

Physical characteristics and composition of pancreatic juice[167]

Volume/day ----------1.500-2.200 ml

Pancreatic juice is clear, colorless, alkaline fluid with strong odor.

pH ---------- 8.0 -8.3

Specific gravity ---------- 1,010 – 1,018

Osmolarity---------- same as plasma

Water---------- 97.6%

Inorganic constituents ---------- 0.6%

Cations: sodium, potassium, calcium, magnesium, zinc
Anions: bicarbonate, chlorides, phosphates, sulphates

Organic constituents ---------- 1.8%

Enzymes: trypsinogen, chymotrypsinogen, procarboxypeptidase, elastase, pancreatic lipase, phospholipase, pancreatic amylase, ribonuclease, deoxyribonuclease, etc.

Albumin and globulin (in traces)

Interesting facts at a glance:

The pancreas produces 1.5 – 2.2 liters (8 – 12 cups) of pancreatic juice daily

The pH of pancreatic juice is between 8.0 – 8.3, thus it is much more alkaline than arterial blood, which has a pH of 7.4

Acidic semi digested food coming from the stomach is called chyme

The bicarbonates found in pancreatic juice neutralize stomach acid in the chyme

The pancreas can take alkaline substances such as minerals and bicarbonate mostly from blood

The higher capacity for a "bicarbonate buffer" in the blood means that it is easier for the pancreatic cells to take bicarbonate from the blood

Pancreatic juice is 97.6% water

Pancreatic juice has the same osmolarity as plasma

The pancreas is the main protein-producing organ in the body

These proteins are digestive enzymes

The pancreas is the key organ of the digestive system

*****

Chapter 3- Decreased Exocrine Pancreatic Function. What are the pancreatic enzymes?

For individuals lacking a medical background

One of the main jobs of the pancreas is producing and releasing the digestive enzymes.

What Are Enzymes?

Enzymes are vital proteins of the body that are necessary for all of life's functions. Without enzymes we could not live. Without them, we simply would cease to function and would die pretty quickly if not immediately. Enzymes are essential to sustain life.

All metabolic and digestive processes that occur within the body require enzymes for them to occur. That is why all the enzymes are conditionally classified as metabolic enzymes or digestive enzymes.

The living cell is the site of tremendous biochemical activity called metabolism. This is the process of chemical and physical changes, which go on continually in the living organism from birth to death.

These processes depend upon the **metabolic enzymes.**

Build-up of new tissue, replacement of old tissue, conversion of food to energy, disposal of waste materials, reproduction, seeing, hearing, feeling, moving, and thinking - all the human activities that we characterize as "life" are dependent on these enzymes.

The role of **digestive enzymes** is to obviously, digest the foods we eat.

These enzymes work by helping take food apart, either by cutting, dissolution, or destruction. When you eat food, our enzymes need to cut the proteins, the fat, and the carbohydrates to small units before the intestines absorb them.

Enzymes are the proteins that speed up specific biochemical reactions in the living cells. Enzymes are the substances that occur naturally in all living cells, including the human organism. Our life is completely dependent on millions of simultaneous biochemical reactions. Enzymes are the catalysts that make these reactions possible because most chemical reactions in biological cells occur too slowly.

Enzyme Assistance

Catalysts are the substances that initiate or accelerate a chemical reaction without being affected or undergoing any permanent chemical change. To work properly, digestive enzymes need essential help. This means that enzymes cannot work without special substances, which are called coenzymes and cofactors. These special substances are mostly vitamins or minerals. Our body cannot produce these substances by itself, but can receive them only from food, water or food supplements.

For an analogy with the car, digestive enzymes are like the spark plugs in a motor. You might have spent thousands of dollars on a new sophisticated car with a powerful engine and fill it up with the best gasoline in the world, but without spark plugs, it won't run! As the weak, bad quality spark plugs can cause serious problems with the motor to burn gasoline, so will the low amount and poor quality pancreatic digestive enzymes not allow the body to properly digest food for energy. Without them, no digestion would take place, just as a car would not run without a sparkplug igniting an explosion, thereby creating energy to move. Moreover, you will stop on the freeway.

Having a low amount and poor quality digestive enzymes means having low energy. It is like driving on only two cylinders instead of six.

There are many digestive enzymes in the mouth, stomach, small and large intestines, but the main organ for manufacturing these enzymes is the pancreas. Some doctors called the pancreas the "host of gastrointestinal tract" for its life important functions. In the future, just for simplicity, the authors will refer to digestive enzymes as pancreatic enzymes.

How Are Enzymes Named?

Digestive enzymes are named based on the substance that they work on and break down. The suffix "-ase" is then affixed to the end of the word.

Protease breaks down proteins to simple amino acids.

Lipase breaks down lipids to simple fatty acids.

Lactase breaks down lactose.

Cellulase breaks down cellulose.

Enzymes come in different types and each enzyme has a special job to do.

Many individuals know about the role of the pancreas in developing diabetes, but don't recognize that the pancreas and pancreatic enzymes are very important for breaking down food into an absorbable, usable form for the body.

Many individuals know the expression "You Are What You Eat," but few realize that a more proper statement will be "You Are What You Eat and Digest".

Without proper digestion, good health is impossible. Even the healthy organic diet will be of little value if the pancreas cannot produce the right amount of high-quality digestive enzymes.

The digestive enzymes (such as amylase, lipase, and protease) are released from the pancreatic cells and flow into the pancreatic duct and then to the duodenum (beginning of the small intestine).

How Can Enzymes Turn a Chicken or a Potato and Pasta Into You?

Digestive pancreatic enzymes literally take food particles apart, piece-by-piece.
Amylase digests carbohydrates; lipase digests fats; and protease digests proteins.
No matter what we eat, we consume mostly proteins, fats, and carbohydrates.

Enzymes digest all of our food and break it into forms of small particles to pass throughout the intestines' wall into the blood. Through this action, digestive enzymes facilitate the digestive process and are essential to the body's absorption and full use of food.

You can make an analogy by imagining an old house with solid bricks and the desire to build another house. The old house is broken down into small bricks and then those bricks are used to build the new house brick by brick. Our body chops up the big molecules of proteins, fats and carbohydrates from food into small parts, which can go through the gut's wall and then be utilized by the body to build up its own tissue. Therefore, our body goes through a similar process when digesting food.

Life could not exist without pancreatic digestive enzymes - thus, they are essential for life.

On one hand, the consumption of vitamins and minerals depends upon pancreatic enzymes, and on the other hand, pancreatic enzymes consist of vitamins and minerals. You have to know, that our body cannot produce the minerals; we can take them only from food, supplements, and healing mineral water. These minerals also help our body to neutralize the acids and keep our inner environment slightly alkaline.

Pancreatic enzymes are extremely sensitive to even the smallest changes in intestinal pH and work only in an alkaline environment. Therefore, the intestines must maintain a proper alkaline pH level. The enzymes do not function properly if the small intestine's pH drops low to acidity levels. The alkalinity of digestive enzymes is an essential part of the digestive process.

Unfortunately, our diet is too high in acid-producing foods like meat, white flour, sugar, alcohol, dairy products, coffee and soft drinks and processed oils and too low in alkaline-producing foods like fresh vegetables and fruits. Chronic inflammation, infection, free radicals, smoking, stress, and a sedentary lifestyle tend to make the body more acidic, as well.

Over-acidity is very common today and can become a dangerous condition that weakens all body systems. Over acidity slowly ruins our cells and our body causing many diseases and premature aging. Alkaline digestive glands, such as the liver and pancreas, suffer from acidic damage most of all. Acidity literally kills the pancreas.

The pancreas works hard and produces 1.5 – 2.2 liters of pancreatic juice daily. The pancreatic digestive enzymes are secreted by the acini cells, which look like berries (acinus is Latin for berry). The duct's cells secrete water and bicarbonate. Pancreatic juice is an alkaline solution with large amounts of minerals such as sodium, potassium, calcium, magnesium and bicarbonate. Alkalinity of pancreatic juice protects the duodenum walls by neutralizing the acidic chyme that comes from the stomach and making the environment for the proper work of pancreatic digestive enzymes, as well.

The chyme entering the small intestine is very acidic due to the hydrochloric acid from the stomach. The acidic chyme sends neural signals (via the vagus nerve) and hormonal signals (via blood messengers: secretin and cholecystokinin) to the pancreas to have large amounts of enzymes fill pancreatic juice into the duodenum. The more acidic the chyme is, the more pancreatic juice is released to neutralize it. Any time the duodenal pH drops below 4.0-5.0, the digestive hormone secretin is released, resulting in the release of bicarbonate in the pancreatic juice.

Pancreas is an alkaline gland

If the body becomes acidic, the biochemistry of pancreatic juice worsens. There are not enough minerals and bicarbonates to neutralize the semi-digested food (chyme), which travels from the stomach into the duodenum. Pancreatic enzymes cannot work in an acidic environment in the duodenum, which causes food to be poorly digested.

Pancreatic enzymes' deficiency is so common in modern society. It is a frequent, real, underlying medical problem behind a whole range of digestive complaints that we accept as "normal."

Digestive disorders are common for millions of Americans. Many of them suffer from stomach discomfort and pain, abdominal cramps, gas, bloating, flatulence, nausea, heartburn, indigestion, constipation or diarrhea, etc. Any or all of these can be symptoms of enzyme deficiency.

In all cases of digestive disorders, there is low digestive function of the pancreas

Many people suffer from chronic fatigue, skin rushes, allergies, food intolerance, overweight and lower weight issues, hormonal and emotional problems, etc.

People suffer from a hidden pancreatic deficiency and don't know that a lack of the digestive enzymes can also increase inflammation and bodily pain and decrease energy and immunity hindering the body's ability to heal wounds and traumas.

Millions of people are continually tired, develop chronic diseases, and age prematurely. In the worse case scenario, they develop cancer. These people most likely have pancreatic deficiency of their pancreatic enzymes and don't realize it.

Without good digestion, there is no good natural health

How can a person survive and have good energy if they are suffering from poor, incomplete digestion? How can the body take partially or poorly digested food and really use it to satisfy the body's cellular, immunity and energy needs? The answer to both questions: the body cannot.

For individuals with a medical background

Enzymes are the proteins that speed up specific biochemical reactions in the living cells. They are fundamental to nearly all biochemical processes. Enzymes are the substances that occur naturally in all living cells, including the human organism.

Our life is completely dependent on millions of simultaneous biochemical reactions. Enzymes are the catalysts that make these reactions possible. Catalysts are the substances that initiate or accelerate a chemical reaction without being affected or undergoing any permanent chemical change. Enzymes are protein molecules that are customized to recognize and bind specific substrates (substrates are reagent molecules upon which enzymes act) and speed their conversion into products. These proteins are responsible for increasing the rates of the many thousands of reactions taking place inside and outside the cells.

The basic enzymatic reaction can be represented as follows: **S + E → P + E**

Where **E** represents the enzyme catalyzing the reaction and it is left unchanged, **S** is the substrate (reactant), the substance being changed, and **P** is the product of the reaction.

Anthony Cichoke in his book "*Enzymes & Enzyme Therapy*" (1994) compares enzymes to the clergy and judges who make and break marriages.[249]

Preachers can initiate the process of marriage and the judge (unfortunately, if you face divorce) breaks the partnership, but the preacher and judge themselves are unchanged by the action.

Enzymes work in the same manner. They start and end the body's biochemical reactions. Our bodies depend on enzymes every second of everyday.

Enzymes perform so many important functions in the body that they have been called "the basis of all metabolic activity." In other words, enzymes deliver nutrients, break down and carry away toxic waste, digest food, purify the blood, deliver hormones, balance cholesterol and triglycerides levels, feed the brain, build protein into muscle, feed and fortify the endocrine system, etc. Enzymes save lives by restoring energy and homeostasis, reversing the aging process, turning a dysfunctional digestive system into a healthy one, and strengthening the immune system, etc.

Enzymes enable our bodies to digest the food we eat. They break down the various foods we consume: proteins, fats, carbohydrates and vitamins into the smaller compounds that the body can absorb. They are essential in maintaining optimal health. When digestion is not properly completed, partially digested proteins putrefy, partially digested carbohydrates ferment and partially digested fats turn rancid. These toxins remain in the body, harming the system. Putrefied, fermented and rancid acidic toxins in the digestive tract can be absorbed into the blood causing inner toxicity, and they are deposited as waste in the fat tissue, vessels, joints and other

areas. The results of enzyme deficiency include digestive and metabolic disturbances, fatigue, headaches, constipation, gas, heartburn, bloating, colon problems, excess body fat, and problems as serious as cardiovascular or heart disease and so on.

There are two basic types of enzymes - systemic/metabolic enzymes and digestive enzymes. Metabolic enzymes catalyze or spark the reactions within our cells. The body's organs, tissues, and cells are enabled by metabolic enzymes, and without them our bodies would cease to function. Digestive enzymes, both found in raw foods and produced by our digestive organs mostly by the pancreas, break down food particles so they can be absorbed.

The medical practice of using the enzymes by mouth for their healing properties shows that enzymes can travel into the whole body system. There is solid evidence that our own pancreatic digestive enzymes can be absorbed into the blood and lymph system for systemic action. This evidence also suggests that digestive enzymes can be absorbed into the blood, re-accumulated by the pancreas, and reutilized, instead of being reduced to their constituent amino acids in the intestines. This is called an enteropancreatic circulation of digestive enzymes.[189]

A deficiency of pancreatic digestive enzymes has a negative impact on both digestive and metabolic processes, thus, there is a negative impact on all functions of the entire organism.

a. Pancreatic digestive enzymes

Basically, pancreatic digestive enzymes are proteins, but of a highly complicated nature.

Some peculiarities of digestive enzymes:

- Enzymes combine briefly with substrates (reactants) during an enzyme-catalyzed reaction

- Many enzymes contain non-proteins groups called cofactors, which contribute to their activity. Inorganic cofactors are all metallic ions include K^+, Fe^{++}, Fe^{+++}, Cu^{++}, Co^{++}, Zn^{++}, Mn^{++}, Mg^{++}, Ca^{++}, and Mo^{++}. Organic cofactors, called coenzymes, are complex groups derived mostly from vitamins. The organism can get the cofactors only from the food, water, and/or nutritional supplements

- Enzymes are saturated by high substrate concentrations

- Enzymes are specific in their activity; each enzyme catalyzes the reaction of a single type of molecule or a group of closely related molecules

- Enzymes are released unchanged after catalyzing the conversion of substrates (reactants) to product. Using systemic enzymatic therapy supports the idea of reabsorbing some of the digestive enzymes into the bloodstream for reuse

- Many digestive pancreatic enzymes are released in the inactive form to prevent the pancreas from self-digestion

b. Factors Affecting Pancreatic Digestive Enzyme Activity

Several factors affect the rate at which enzymatic reactions proceed.

1. **Temperature.** The "optimum" temperature for human enzymes is usually between 35 and 40 degrees C. The average temperature for humans is 37 degrees C.

2. **pH.** Extremely high or low pH values generally result in the complete loss of activity for most pancreatic digestive enzymes. pH is also a factor in enzyme stability. As with activity, there is also a region of pH optimal stability for each enzyme.

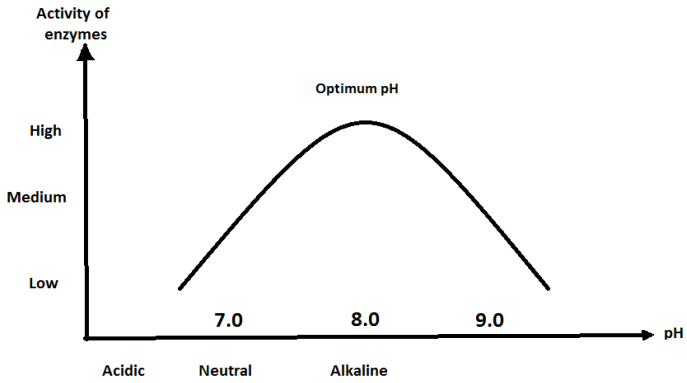
Optimum pH for Activity of Pancreatic Digestive Enzymes[170]

Lipase = 8.0

Trypsin = 7.8 - 8.7

Amylase = 6.7 - 7.0

Normally, digestive enzymes have a pH optimum for maximum activity. Changes in pH in the small intestine can change the activity of the pancreatic enzymes.



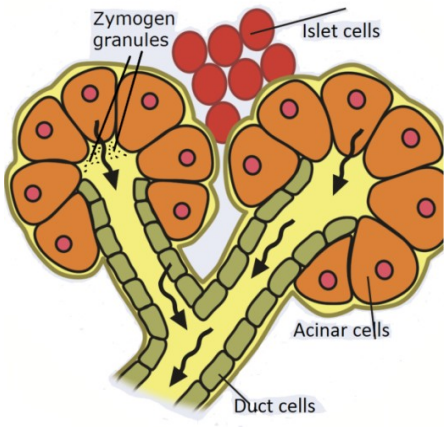
3. **Enzyme concentration.** Concentration of digestive pancreatic enzymes depends upon many factors such as nervous and hormonal regulation, normal structure and function of the pancreas and the proper amount of nutrients (protein, vitamins, minerals, trace elements, bicarbonates, water and more) to produce digestive enzymes.

4**. Substrate concentration**. The exocrine pancreatic function is adapted to the composition of nutritional substrates. Producing and releasing the pancreatic digestive enzymes depends on substrate concentrations in the food. Proteins in the food stimulate releasing pancreatic juice with more concentrations of trypsin and lipids (fats) causing more concentration of lipase. Chewing, frequency of eating, the amount of food consumption, osmolarity of food mass, dehydration and fasting have a strong influence on the substrate concentration, and thus, on the exocrine pancreatic function.

5. **Presence of enzymes' inhibitors or activators.** Enzyme inhibitors are substances which alter the catalytic action of the enzyme and consequently slow down, or in some cases, stop catalysis. The binding of enzyme inhibitors to enzymes can be reversible or irreversible.

Alcohol, tobacco, many recreational drugs and some medications, environmental toxins and gastrointestinal dysbiosis practically inhibit the exocrine pancreatic function and trigger the pancreatic disorders.

Pancreatic juice is a combination of acinar cell and duct cell secretions. About 40 acinar cells are arranged into a spherical unit called an acinus. An acinus (adjective: acinar, plural acini) refers to any cluster of cells that resembles a many-lobed "berry," such as a raspberry (*acinus* is Latin for berry).



View of the human pancreas shows clusters of acinar cells (i.e., acini), islet cells (i.e. islets), zymogen granules, and pancreatic ducts.

The acinar cells secrete amylase, proteases, and lipases - enzymes responsible for the digestion of all three food types: carbohydrates, proteins, and fats. The acinar cells are pyramid-shaped, with their apices facing the lumen of the acinus. Near the apex of each cell are numerous enzyme-containing zymogen granules that fuse with the apical cell membrane.

The centroacinar and duct cells secrete the water and electrolytes present in the pancreatic juice. These cells contain the enzyme carbonic anhydrase, which is needed for bicarbonate secretion.

As you can see, digestive pancreatic enzymes do more than just aid digestion.

c. Insufficiency and deficiency of pancreatic amylase

Amylase refers to a group of enzymes whose catalytic function is to hydrolyze (breakdown) sugar and starch. Amylase is the only pancreatic enzyme secreted in its active form. Amylase

digests carbohydrates (polysaccharides) into smaller disaccharide units, eventually converting them into monosaccharides such as glucose, which are then absorbed into the blood.

Specific pancreatic enzymes that aid in digestion of carbohydrates:

Enzymes => => => => => => => => => Substrates

Amylase splits **Carbohydrates** (starches and other polysaccharides) to **Disaccharides**.

Disaccharides are lactose, sucrose, and maltose.

Lactase splits **Lactose** (milk sugar) to **Glucose + Galactose** (monosaccharides)

Sucrase splis **Sucrose** (table sugar) to **Glucose + Fructose** (monosaccharides)

Maltase splits **Maltose** (malt sugar) to **Glucose + Glucose** (monosaccharides)

Amylase Deficiency: Amylase digests carbohydrates along with dead white blood cells. Amylase is also involved in anti-inflammatory reactions such as those caused by the release of histamine and similar substances. An amylase deficiency can result in skin problems such as psoriasis, eczema, atopic dermatitis, hives, allergic reactions, and all types of herpes. Asthma and emphysema may also be exacerbated by an amylase deficiency. Many people who suffer from skin rushes, allergies, sinusitis, poor microcirculation, aching neck/shoulders/back, chronic inflammation, fatigue and/or depression may have pancreatic amylase deficiency.

Lactase Deficiency. People with milk intolerance usually have classic symptoms of lactase deficiency, which include abdominal cramps and diarrhea. Other allergic symptoms, including sinusitis, bronchitis and asthma, have been witnessed from the ingestion of lactose (milk) - containing products.

Maltase Deficiency can cause sensitivity to environmental conditions.

In rare cases of **Sucrase (invertase) deficiency**, the sucrose disaccharide cannot be split into two units of glucose and fructose. Glucose is a primary brain food so deficiency of this pancreatic enzyme may cause mental and emotional problems in people who cannot get glucose into the brain. Symptoms may include depression, moodiness, panic attacks, and severe mood swings.

d. Insufficiency and deficiency of pancreatic protease

Proteases are the pancreatic proteolytic digestive enzymes (proteolysis - the hydrolysis of proteins into peptides and amino acids by cleavage of their peptide bonds). Proteases are needed to digest proteins, which are among the most complex organic compounds found in nature. Every animal, including humans, must have an adequate source of protein in order to grow and maintain itself. Proteins, which build with blocks of many amino acids, are the fundamental

structural elements of every cell in the body. Thus, protein well deserves its name, which is of Greek, meaning "of first importance."

Proteins in our diet are derived from either animals such as meat, eggs, milk, fish or from plants such as vegetables, nuts and seeds. Proteins are long chains of amino acids held together by peptide bonds. Proteins, in the beginning, are predigested in our stomach and then protein's digestion occurs in the small intestine, where proteolytic enzymes secreted by the pancreas further break down the proteins.

At first, proteases break down proteins to polypeptides (big blocks of amino acids).

Second, the proteases chop up the polypeptides into the amino acids. Amino acids are then absorbed into the blood.

Trypsin, chymotrypsin, and carboxypolypeptidase are the most important of the proteases secreted by the pancreas

Specific Pancreatic Enzymes That Aid Digestion Proteins

Enzymes => => => => => => => => => **Substrates**

Trypsin => => => splits => => **Proteins** to => => => **Peptides** (big blocks of amino acids)

Chymotrypsin => splits => => **Proteins** to => => => **Peptides**

Elastases => => splits => => => **Proteins** to => => => **Peptides**

Nucleases => => splits => => =>**Proteins** to => => => **Peptides**

Carboxypolypeptidase splits =>**Peptides** to =>free **Amino Acids**

If proteins are not properly broken down before they are absorbed, various health consequences may occur.

Proteases from the pancreas are able to hydrolyze almost all proteins as long as they are not components of its own body's living cells. Pancreatic living cells are protected against self-digestion by the very complicated inhibitor mechanism. Acinar cells themselves are highly resistant to trypsin and chymotrypsin.

What Are Zymogens?

Zymogens are enzymes that are secreted in an inactive form. They are also called proenzymes (precursors of enzymes). Under certain conditions, zymogens shift to the active form of the enzyme. Generally, zymogen secretions happen because the enzyme activity inside the pancreas can harm its own pancreatic tissue. For example, a well-known zymogen is trypsinogen, which is secreted by the exocrine pancreas and which becomes an active trypsin enzyme.

Trypsin is the major pancreatic protease, which is synthesized and packaged into secretionary vesicles (zymogen granules) as the inactive proenzyme, trypsinogen. Trypsinogen is converted to its active form, trypsin, by another enzyme, enterokinase, which is produced by the duodenal mucosal cells. Trypsin, in turn, activates the other proteolytic enzymes. Trypsinogen activation within the pancreas is prevented by the presence of inhibitors that are also secreted by the acinar cells. Inhibition of trypsinogen activation ensures that the enzymes within the pancreas remain in an inactive precursor state and are activated only when they reach the duodenum. If inhibitors of proteases lose their activity, proteases can digest their own tissue, causing cellular damage and pancreatitis.

Parasites, fungal forms, and bacteria are proteins. Viruses are cell parasites consisting of nucleic acids covered by a protein film. Proteases can break down undigested protein, cellular debris, and toxins in the blood, sparing the immune system this task. The immune system can then concentrate its full action on the bacterial, yeast or parasitic invasion. Therefore, pancreatic protease deficient people are immune compromised, making them susceptible to frequent and chronic bacterial, viral and Candida-yeast infections, and a general decrease in immunity.

Lopez D.A. *et al.* (1994) considered that this mechanism may also help the body to prevent the growth and spreading of the cancer cells.[73,74] Proteases can make the cancer cells more vulnerable to the killing actions of immune cells. In other words, proteases remove camouflage from cancer cells, making them visible for attacks from our immune system.

The proteases are important in preventing tissue damage during inflammation and the formation of fibrin clots. Pancreatic protease deficiency makes it difficult to heal the wounds, sports injuries, tendinitis, chronic inflammatory conditions, etc.

Some authors consider that protease deficiency can also lead to edema – fluid retention and swelling of the hands and feet. Poor protein digestion and absorption can lead to production of toxic substances in the colon (toxic colon) and an increased risk of intestinal infections.

Normally, pancreatic juice has a strong antibacterial activity against a whole spectrum of microorganisms. This action depends on trypsin. This antibacterial activity can be halted by the trypsin inhibitor.[150] Pancreatic juice in healthy individuals and animals has antibacterial and antifungal activity.[149, 150] This is why a healthy pancreas is resistant to bacterial infection. [152]

Trypsin and possible other proteases play significant roles to keep the small intestine free from a large amount of bacteria and parasites. A lack of pancreatic proteases greatly increases an individual's risk of having an intestinal infection including Small Intestinal Bacterial Overgrowth and chronic Candida-yeast overgrows in the gastrointestinal tract.

This activity is also highly sensitive to changes in pH with maximum activity at pH 8.5 (alkaline) and completed at the end of action at 7.0 (neutral).[148, 149,] Laubitz D, Zabielski R *et al.* (2003),[152] also have shown that the antibacterial factor was absent when the juice pH was getting below 8.0.

Protease is required for separation of vitamin B12 from protein. Festen HP (1991) [201] concluded that pancreatic insufficiency may lead to cobalamin (vitamin B 12) deficiency.

e. Insufficiency and deficiency of pancreatic lipase

Fats (lipids) are one of the three major food groups needed for proper nutrition. Fats are an important source of energy and an important component of our diet since fats form the basis of many hormones and cell membrane building blocks. Fats require special digestive action before absorption because the end products must be carried in a water medium (blood and lymph) in which fats are not soluble.

Lipase is the pancreatic digestive enzyme needed to digest fat and to split fats into fatty acids and glycerol (to be converted into glucose). Lipase requires a high pH for its activation among food enzymes.

Pancreatic bicarbonate secretion is diminished in exocrine pancreatic deficiency. Therefore, low amounts of bicarbonate in the pancreatic juice cannot protect pancreatic enzymes from being denaturized by gastric acid. Low duodenal pH dramatically reduces lipase activity (only 50% activity at pH 7.0 compared with pH 9.0). [68] Pancreatic lipase can be inactivated irreversibly by acidic pH (that is pH 4).[71]

Fats are the most difficult of all foods to digest. Emulsification is the real key to the proper digestion of fats. The large fat particles present comparatively small surfaces for the lipase to work on, so the process of emulsification by the action of bile, produced by the liver, is necessary. Bile breaks down the large fat particles to tiny droplets, which provide lipase with an enormously increased surface to work on. Emulsification allows lipase to gain easier access to the fat molecules and thus accelerates their breakdown and digestion.

If the amount of bile is insufficient, the pH of bile is in decline, and there is a problem with proper elimination of bile or, if the liver is not stimulated to produce bile, fats remain as large particles. Therefore, fat digestion is incomplete and fat absorption is markedly reduced. So, normal digestion and absorption of dietary fat is critically dependent on secretions from both the pancreas and liver.

If fats (lipids) are not properly broken down before they are absorbed, some health consequences may occur. A shortage of lipase results in malabsorption of fats and fat-soluble vitamins. Lipase digestion is of paramount importance for the well being of the individual. A deficiency of lipase causes high cholesterol, high triglycerides in the blood, fatty liver, weight gain and diabetes. Lipase deficient individuals have decreased cell permeability, meaning nutrients cannot get into the cells and the waste cannot get out of the cells.

The inability to digest fat interferes with insulin metabolism and the transport of glucose into the cell by insulin. Diabetics are lipase deficient and cannot get glucose into their cells, nor can wastes or unwanted substances get out.

Lipase-deficient people may also be deficient in many fat-soluble nutrients, including vitamins A, D, E and K. This is why individuals with pancreatic deficiency may also have bone pain, muscle cramps, night blindness and easy bruising.

Specific Pancreatic Enzymes That Aid Fat Digestion

Enzymes and Bile => => => => => => => => => **Substrates**

Lipase => => => => splits **Fats** => => => => => to **Fatty Acids** and **Glycerol**

Phospholipase => => splits **Phospholipids** => => to **Fatty Acids**

Cholesterol esterase splits **Cholesterol esters** => => to **Fatty Acids** and **Cholesterol**

There is also a tendency amongst individuals suffering from being lipase deficient, to have a problem with electrolyte balance, as well. People with a deficiency of pancreatic lipase may have an increased propensity toward calcium, zinc, and iron deficiencies. Lipase can also help to destroy some viruses by digesting their outer coating, thus, making these viruses an easy target for the immune system.

Some authors consider that an important indicator of lipase deficiency is chronic fatigue, sore throat and swollen glands. Muscle spasms and a spastic colon are also reported as being symptoms of lipase deficiency.

In severe pancreatic deficiency, when the pancreas produces less than 10% of lipase, fats are not properly broken down and travel to the stool without being absorbed. In this situation, many health consequences may occur.

People with severe pancreatic deficiency may have excess oil in the stool (steatorrhea). This is associated with symptoms of pale yellow, foul-smelling, greasy, bulky stools that stick to the side of the toilet bowl or are difficult to flush or oil droplets floating in the toilet bowl after bowel movements.

Individuals with pancreatic lipase deficiency may also have feelings of fullness, abdominal tenderness and pain, gas, bloating, loss of appetite, diarrhea, and weight loss.

Pancreatic deficiency is a very complicated condition and usually has a tendency for progression. Deficiencies of protease, amylase, lipase, bile, and lack of stomach hydrochloric acid are all interrelated. The stomach, duodenum, pancreas, liver, and gallbladder work together as a well trained and organized orchestra of digestion under conduction of the nervous and hormonal systems. Every organ depends on each other, but the pancreas plays the most important role, which cannot be under estimated.

f. Three stages of Decreasing of Exocrine Pancreatic Function are

"*Acidic pancreas and bile*", "*Pancreatic Deficiency*," and "*Pancreatic Failure*"

Most of digestion and absorption takes place in the small intestine and is mediated by the pancreatic digestive enzymes: amylase, protease, lipase, as well as bile from the liver. Without proper enzyme production, the body has a more difficult time digesting food, which may lead to a variety of chronic disorders.[66]

Enzymes produced by the pancreas are responsible for the digestion of 50% of all carbohydrates, 50% of all protein, and 90% of all fat. In addition, the bicarbonate produced by the pancreas is essential for neutralizing the acidic chyme passing into the duodenum from the stomach. A deficiency or low activity of digestive pancreatic enzymes leads to indigestion with many subsequences.

Common symptoms of chronic pancreatic deficiency include abdominal bloating and discomfort, gas, indigestion, and the passing of undigested food in the stool. For laboratory diagnosis, most nutrition-oriented physicians use *Comprehensive Digestive Stool Analysis*. Another indicator of pancreatic insufficiency is the intestinal overgrowth of the yeast *Candida albicans*.[67]

Moreover, it has to be taken into account that in states of chronic digestive enzyme deficiency, complex and interacting alterations of secretion, motor, and endocrine functions may contribute to symptoms, which may even precede over malabsorption.[72]

In medical literature, many terms are used to describe this severe pancreatic disorder: pancreatic enzyme deficiency, digestive enzyme deficiency, exocrine pancreatic deficiency, exocrine pancreatic insufficiency, maldigestion disorder, pancreatic insufficiency, malabsorption, etc. All these terms describe the same and severe pancreatic disorder.

All these expressions reflect the different stages of the condition or various severity levels of the same process, when the pancreas cannot produce the proper amount of high-quality digestive enzymes. Many of these medical terms do not define a clear understanding, confuse individuals, and most importantly, do not reflect the stage and severity of this pancreatic disorder, nor provide possible healing or treatment actions.

These medical terms focus only on the latest stage of exocrine pancreatic deficiency (malabsorption) and waste crucial time when this condition can be reversed or properly treated to postpone the exacerbation and progression of the deficiency. The malabsorpton syndrome is the decompensated and final stage of exocrine pancreatic deficiency and the failure of the pancreas, when the therapeutic possibilities of experts and doctors appreciably are limited.

Can we prevent the inevitable – the progression of the beginning of pancreatic insufficiency into pancreatic failure? Our answer is "yes"

The pancreas is truly a workaholic gland with a huge 10-fold capacity. Thus, malabsorption, which is described usually as a "pancreatic insufficiency" occurs after pancreatic enzyme secretion is reduced more than 90% and only 10% of normal lipase activity is left.

This rarely happens overnight. Pancreatic deficiency develops more slowly. For many individuals, approximately 8-15 years take place between the first attack of acute pancreatitis to when the pancreatic function will be totally destroyed.

Sorry to say, but for everyday situations we don't have simple and useful tests or procedures, which can catch the early, functional stage of exocrine pancreatic deficiency. This is important, because most of functional gastrointestinal disorders have a deep connection with impaired function of the pancreas.

Low exocrine pancreatic function is a cornerstone of almost all gastrointestinal disorders and illnesses

Very often, symptoms of diminished exocrine pancreatic function overlap with symptoms of gastritis, dyspepsia, GERD, ulcers, IBS, Sphincter of Oddi Dysfunction (SOD), Celiac Disease, Candida-yeast overgrow, Crohn's Disease, hepatitis, gallbladder inflammation and stones and so on.

The pancreas is the forgotten organ particularly because conventional medicine does not have a real solution to increase the exocrine pancreatic function by traditional treatment. Usually, this vital organ is only paid attention to when is too late and time for proper action to heal the pancreas is gone.

In everyday practice, it is very difficult to identify the early stages of exocrine pancreatic deficiency when the process can be reversed, thus, this condition is generally missed.

In this book, the authors discuss practical conception of developing a course focused on, healing of pancreatic disorders. The authors are more focused on history and clinical symptoms to reveal the beginning of this condition. In many cases the *Comprehensive Digestive Stool Analysis* is also helpful.

The authors completely agree with John Alfred Lott, who wrote in his book *Clinical Pathology of Pancreatic Disorders* that generally, pancreatic insufficiency is graded as mild when only bicarbonate output is decreased, moderate when enzyme output is also decreased, and severe

when fecal fat output is increased (steatorrhea).”[3] Other authorities of pancreatic health share this idea.[68]

Some experts, including Harada H. *et al.* (1978), consider that bicarbonate output may be used as a marker of the exocrine pancreatic dysfunction. [69] Decreased bicarbonate secretion eventually results in decreased duodenal pH.

Furthermore, Rinderknecht H. (1993) suggests in his book, *The Pancreas: Biology, Pathobiology and Disease*, that decreased bicarbonate secretion from the pancreas eventually results in decreased duodenal pH. This is important because an alkaline duodenum pH is a prerequisite for the optimal activity of digestive enzymes.[70]

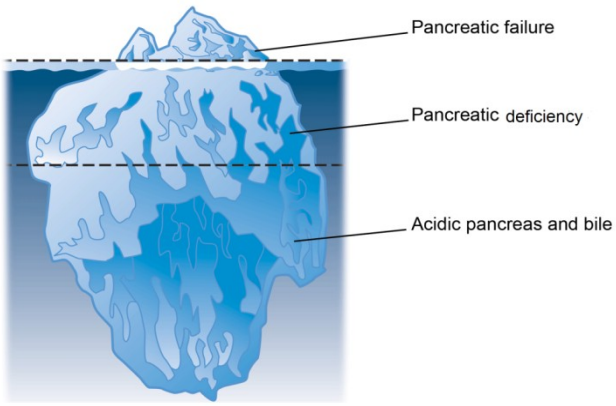
g. Exocrine Pancreatic Deficiency

Exocrine pancreatic deficiency is prevalent in modern population and it is large correlated with widespread of digestive disorders. The beginning of the process, the functional stages are usually under diagnosed. The severe cases are just the tip of the iceberg.

By the authors’ opinion, for the most common chronic situation, exocrine pancreatic deficiency can be divided in three stage of this disturbance.

1**. *Acidic pancreas and bile***: Pancreatic juice and bile become more acidic and pH of pancreatic-bile secretion drops.

What usually happens in this beginning stage? For many reasons, the amount of bicarbonates and minerals in pancreatic juice and bile diminish. In turn, this causes deep biochemical and biophysical changes in the pancreas, pancreatic juice and bile. Activity of pancreatic digestive enzymes and bile becomes low. Pancreatic juice and bile cannot properly neutralize the chyme and the environment in the duodenum becomes acidic.



Because the pancreatic enzymes work only in alkaline conditions, they lose their activities when an acidic condition is present. This causes, in its turn, a chain reaction of symptoms:

- Improperly digested food starts to ferment and putrefy, causing gas, distention, bloating, cramps, constipation or loose stool

- Indigestion due to low activity of pancreatic digestive enzymes leads to nutritional deficiencies, fatigue, allergies and inner toxicity

- Acidic conditions in the duodenum cause precipitation of bile salts into the bile acids. Chemically aggressive bile acids irritate and erode the mucous membrane of the duodenum causing spasms and bile reflux into the stomach, esophagus and back to the pancreatic duct. This irritation leads to refluxes, ulcers of the duodenum or the stomach or the developing of acute pancreatitis

- Proper amount and normal activity of bile and pancreatic enzymes normally control the multiplying of bacteria, parasites and Candida - yeast in the small intestine. Reduction of bile and pancreatic antibacterial activity due to acidic changing has the exact opposite effect

- Low amounts of bile equal low activity of lipase and subsequently low digestion of fat and fat-soluble vitamins such as A, D, E, and K

This functional stage can be reversed.

Millions of Americans suffer from a variety of functional gastro-intestinal disorders including abdominal pain, stomach discomfort, cramps, gas, bloating, heartburn, cravings, indigestion, alteration in bowel habits, etc. Many people have chronic fatigue, allergies, food intolerance, overweight and underweight issues, etc. These individuals most likely have an *acidic pancreas and bile* stage. Their pancreases still produce enough digestive pancreatic enzymes, but, the acidic environment decreases the activity of these enzymes due to the lowering of bicarbonate and minerals in the pancreatic juice and the gut, causing many GI disturbances. Many of these individuals have mild pancreatic deficiency and don't realize it. Their tests are normal and they receive a diagnosis such as functional dyspepsia, IBS or gastritis without any attempt to improve the exocrine pancreatic function. Some of these sufferers are labeled as pshycho-somatic and are treated accordingly.

2. ***Pancreatic Deficiency***: The second stage is the moderate exocrine pancreatic deficiency, where the process begins to injure the pancreas and diminish the activity of pancreatic tissue. However, the organism attempts to compensate this damage. Normally, the functional capacity of the pancreas is 90%. It means that even 10% of pancreatic function may keep organism alive. When moderate exocrine pancreatic deficiency ensues, the pancreas works at max functional capacity to attempt to fight off this condition.

In the *pancreatic deficiency* stage, all the problems described above, are significantly aggravated. Tissue damage can cause attacks of pain in epigastria and indigestion.

The first alarming bell can be an attack of acute pancreatitis with pain, nausea, severe abdominal distention, fever, etc. In many cases, the diagnosis of acute pancreatitis is confirmed in the hospital, but a large number of mild forms can be misdiagnosed. Even if the individual after this attack feels well anyway, the countdown clock starts ticking and this individual is at a high risk of developing moderate and severe exocrine pancreatic deficiency.

This is a very important time when the process can be reversed or stable remission may be achieved. At that time, one requires the persistent healing action and lifestyle change to prevent *pancreatic failure*.

The stage of *pancreatic deficiency* can be diagnosed by medical history, symptoms, lab tests and diagnostic procedures.

Hundreds of thousands of individuals in the US suffer from this problem. They can eat a healthy diet, but the body will not properly utilize the nutrients from the food. Their organisms are literally starving. Without the proper amount of their own pancreatic digestive enzymes, individuals suffer from a deficiency of nutrients and essential minerals, trace elements and vitamins. Serious disturbances form in the nervous and hormonal system, as well. *Pancreatic deficiency* usually combines with intestinal dysbiosis because of either diminishing antimicrobial activity of pancreatic juice and bile and/or overusing antibiotics.

Pancreatic deficiency stage is moderate exocrine pancreatic deficiency that begins in many cases after the first attack of pancreatic pain and is usually accompanied with nausea, bloating, diarrhea, indigestion, etc.

Exocrine pancreatic deficiency also occurs in early stages of cystic fibrosis, chronic alcoholism or biliary pancreatitis and after surgeries of the gastrointestinal tract in which portions of the stomach, gallbladder, pancreas, or something else is removed. Certain gastrointestinal diseases, such as stomach and duodenum ulcers, severe GERD, Sphincter of Oddi Dysfunction (SOD), celiac disease, and early Crohn's disease, skin and autoimmune disorders may contribute to the development of exocrine pancreatic deficiency or, by the authors' opinion, may be the result of this moderate pancreatic enzymes deficiency.

3. ***Pancreatic failure***: The third and final stage and similar to heart and kidney failures, is the severe condition requesting many serious medical and healing methods.

Most medical professionals traditionally call this condition "pancreatic insufficiency" or "malabsorption syndrome". Medically speaking, it is not the insufficiency; it is the decomposing stage of exocrine pancreatic deficiency when less than 10% of pancreatic function remains. Severe metabolic disturbances causing weight loss, deficiencies of essential nutrients, the occurrence of loose stools containing unabsorbed fat (steatorrhea), and severe inner toxicity is presented in this pancreatic failure. It is now easy to diagnose this condition by tests and diagnostic procedures, but very difficult to treat.

Interesting facts at a glance:

“You Are What You Eat and Digest”

Without proper digestion, good health is impossible

The pancreas produces and releases digestive enzymes such as amylase, lipase, and protease. Amylase digests carbohydrates; lipase digests fats; and protease digests proteins

The body’s absorption of vitamins and minerals depends upon enzymes and, on the other hand, the work of enzymes requires the body to supply the right amount of vitamins and minerals to the pancreas

The pancreas is an alkaline gland. The alkalinity of the pancreas is an important aspect of digestion, and it is also a main feature regarding the antibacterial activity of pancreatic juice

Acidity literally kills the pancreas

Low digestive function of the pancreas is found in all cases of digestive disorder

Exocrine pancreatic deficiency is a very complicated condition and has a tendency to worsen

Can medical professionals prevent pancreatic deficiency from evolving into pancreatic failure? The answer is "yes"

The three stages detailing the Decrease of Exocrine Pancreatic Function are *Acidic Pancreas and Bile*, *Pancreatic Deficiency*, and *Pancreatic Failure*

*****

Chapter 4-Acidity Kills the Pancreas

For individuals lacking a medical background

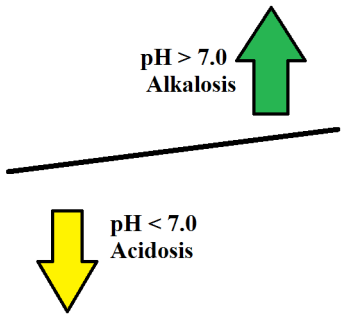
From school everybody knows that there are acid and alkaline solutions. Scientists developed a special measuring of these conditions by using a pH scale from 0 to 14. Just as the mile is a measure of distance, and the hour a measure of time, the pH unit measures the degree of acidity or alkalinity of a solution. Pure water is neutral and has pH of 7.0. Below 7.0 shows that this solution is acidic; a pH of 0 is the most acidic. On the other hand, a pH higher than 7.0 shows that this solution is alkaline; a pH of 14 is the most alkaline.

In this book we will often use words “acidity” and “alkalinity” to simply describe levels of pH. For example, if acidity increases, alkalinity diminishes, but don’t be confused with pH when these relations are opposed.

(Most Acidic) **0**---------- **7** (Neutral) ---------- **14** (Most Alkaline)

pH is lower than 7.0 = Acidity---------- pH is higher than 7.0 = Alkalinity.

More Acidity means less Alkalinity----------Less Acidity means more Alkalinity



It must be remembered that when acidity increases, the pH decreases, contrary, when acidity decreases, the pH increases

The human body keeps proper (slightly alkaline) acid levels– alkaline balance, especially in the blood. The pH of our blood is constantly 7.4. If the blood's pH drops to 7.0 all vital organs such as the heart and brain will stop working and death ensues. That is why our body has a very smart mechanism to keep pH of the blood only 7.4, not higher, nor lower.

When people are asked about acidity in the body, some of them point to the stomach. Normally, acid in the stomach helps us to digest the proteins, minerals and some vitamins.

Whole body acidity is something different. This refers to our cells living, breathing and making waste. These waste products usually are acids. As fire produces smoke, so does metabolism produce acid - CO2 (carbon dioxide) and metabolic acids. If the body receives too much acidic food or too many acids are manufactured by our cells, or body cannot neutralize or remove these acids, all our cells bathe in their waste. This condition is called over acidity, or acidosis.

Like acid eating into marble, acidosis erodes and eats into cell wall membranes of the heart, brain, arteries and veins. Over acidity slowly kills our cells and our body, causing many diseases and premature aging.

The whole body acidity makes the body's fluids acidic also, so the bile and pancreatic juice become acidic, as well. Their biochemistry is changing and they are getting "sick". We call this condition *acidic pancreas and bile*.

a. Four *Acidic Pancreas and Bile* Problems

Four huge problems develop in this condition.

First, bile and pancreatic juice become "aggressive" and irritate surrounding tissue causing spasms, pain, ulcers, refluxes, inflammation, precipitation of the stones and even cancer.

Second, in case of *acidic pancreas and bile* there are changes of the biochemistry of pancreatic juice and bile, hence decreasing the activity of pancreatic digestive enzymes. These enzymes can

work only in an alkaline environment (pH 7.5 – 8.5). Acidity shuts off the digestive process. If digestive enzymes cannot properly digest the foods we eat, many gastrointestinal disorders develop. Indigestion causes deficiency of essential nutrients, which influence the work of nervous, hormonal, cardiovascular, immune, muscle, skeletal systems and so on. Everything starts to go wrong.

Third, digestive enzymes are usually inactive inside the pancreas, but an acidic environment can make them active inside the pancreas. Then, big trouble ensues. Activated inside the pancreas, the pancreatic enzymes start to digest their own pancreas causing pancreatitis.

The fourth problem includes the lowering of antimicrobial activity of pancreatic juice and bile. This may be caused by acidity. If this happens, Candida-yeast and other microbes and parasites make a habitat in the small intestine, thus, totally stopping the normal digestion. On the other hand, unfriendly intestinal micro flora makes the body more toxic and acidic then before.

b. Pancreas and Acidity

The pancreas is an alkaline gland. The pancreatic juice is an alkaline solution with pH in the region of 7.1 - 8.3. This is essential for digestive pancreatic enzymes, because they only work in this range of pH. Alkalinity of pancreatic juice proportionally depends on the amount of minerals and bicarbonate in it.

From where do pancreatic cells take the minerals and bicarbonate to make the pancreatic juice alkaline? The scientists consider that they are mainly taken from the blood. In case of a deficiency of those minerals and bicarbonate in the body, the blood becomes “greedy” and doesn’t let them go into the pancreas, causing *acidic pancreas and bile*.

Blood pH is constant at 7.4 and the whole body makes great efforts to keep it stable. It is known, that even a small change of blood pH below 7.0 causes a shutdown of the heart, lungs, and brain – the life essential organs, and death of the whole organism.

To avoid that, our body and, especially our blood, have a buffer system that prevents the decreasing of pH below 7.4. A "buffer” is a type of device that acts chemically to resist changes in pH. Buffers act against all pH changes to keep the blood pH constant.

It is most important that the buffer system includes bicarbonate in the blood. Bicarbonate is one of the major buffering systems used to maintain the pH of body’s blood.

There is a little chemistry to understand the action of the bicarbonate buffer system. Normally our cells breathe by taking in oxygen and releasing carbon dioxide - CO2.

When carbon dioxide dissolves in water, it can do so as a gas dissolved in water or by reacting with water to produce carbonic acid. In the cells of your body, the rate of carbonic acid production is accelerated by the enzyme carbonic anhydrase, as indicated in the following figure.

$CO_2 + H_2O \Longleftrightarrow H_2CO_3 \Longleftrightarrow H^+ + HCO_3^-$

Carbonic acid is known as a weak acid because it partially dissociates into the positive hydrogen ions and negative bicarbonate ions. The reactions are reversible.

When excess hydrogen ions are added to the system causing too much acidity, the equilibrium is shifted to the left. This means that some of the added hydrogen ions will react with the bicarbonate ions to produce carbonic acid and the carbonic acid will dissociate into carbon dioxide and water as shown below.

Excess **H+** ions shifts this chemical reaction to the left

$CO_2 + H_2O \leftarrow H_2CO_3 \leftarrow H^+ + HCO_3^-$

The more bicarbonate there is, the more alkaline the body is. The lungs and kidneys respond to pH changes by removing CO_2, HCO_3^-, and H^+ from the blood. To assist the buffer system and to keep the body slightly alkaline, minerals such as sodium, potassium, calcium and magnesium are required. It also needs CO_2, and H^+ to be removed from the blood.

Over-acidity is very common today and can become a dangerous condition that weakens all body systems. This condition forces the body to borrow alkaline minerals, including calcium, sodium, potassium, and magnesium from muscles and bones to neutralize acid and remove it from the body. Over-acidity can go undetected for years and cause severe damage. Acidosis is the first step towards premature aging and accelerated oxidative stress.

Fortunately, our bodies have a regulating system preventing us from becoming too acidic. This system includes the alkaline minerals, such as sodium, potassium, calcium, and magnesium both inside and outside the cells. There are large amounts of minerals stored within our bones.

In an acidic situation, calcium leaves the bones, goes into the blood, and precipitates inside the vessels and inner organs, especially into the pancreas. Calcium inside the pancreas produces the small stones, which close the small and big pancreatic ducts. Doctors can see the calcium deposits inside the pancreas in many patients with chronic pancreatitis by using an X-ray.

We also have a buffer system or alkaline reserve in the blood that helps to keep its pH constant. The bicarbonate buffer in the blood is extremely important.

Our body has only one way to rescue itself from acidity - to get more minerals and bicarbonates to neutralize over acidity

Where does the body get them? Our body does not produce the minerals and bicarbonate we need; we can receive them only from food, water, healing mineral water or mineral supplements.

Minerals such as sodium, potassium, calcium, magnesium, and bicarbonates created the body’s alkaline reserve to prevent shifting to the deadly acidic level.

The great alkaline reserve is the body's bank account. The body can call upon it anytime to release alkaline elements for the neutralization of acid. However, there is not an endless supply of bicarbonate and minerals ions available to neutralize the damaged acid–alkaline balance. The alkaline reserve is limited, and it is only a back-up system to keep from poisoning the body with

too much acid-forming food. When this alkaline reserve is depleted, the body sickens and death follows.

The body must maintain the pH of the blood within a narrow range at all times otherwise death will quickly ensue.

Unfortunately, chronic body acidity is very common today because of our "acidic" life style. This is our pay for urbanization. The fundamental cause of most disease is the artificial environment we have created. That environment includes the air we breathe, the water we drink, the food we eat, and the lifestyle we enjoy. We are genetically adapted to living outside, breathing fresh air, drinking clean water, and eating foods exactly as they are found in nature after considerable physical effort is made in obtaining them.

One of the important factors of acidity is modern food and our way of eating. Most of what we eat now is acidic in nature and, therefore, changes the balance toward the acidity condition called metabolic acidosis.

Scientists proved that people now are more acidic by comparison with our ancestors. Most of modern men now have a deficiency of bicarbonate, potassium and magnesium, the main ingredients for neutralizing the acid radicals.

Our diet is too high in acid-producing foods like meat, white flour, sugar, alcohol, most dairy products, coffee and soft drinks, processed and refined vegetable oils, and too low in alkaline-producing foods like fresh vegetables and fruits. Infection, smoking, stress, and a sedentary life style tend to make the body more acid.

Many scientifically based medical researches support the authors' belief that maintaining the alkaline design of the body is the key to common health and vitality. On another hand, *acidic pancreas and bile* is the underlying cause of many if not all gastrointestinal disorders, therefore negatively influencing whole body's health.

For individuals with a medical background

In this chapter, it will be attempted to understand the connection between the acid – alkaline, or the acid – base, balance of the body and health of the pancreas, or in other words, between chronic metabolic acidosis and pancreatic disorders.

Chemistry

First, let us describe the terms acidity and alkalinity and review some basic chemistry. In terms of chemistry, when one talks about acidity or alkalinity, one is talking about the hydrogen ion. An acid is a substance that releases a hydrogen ion into a solution and an alkaline substance is

one that removes a hydrogen ion from a solution. The pH (potential of hydrogen) is a measure of the acidity or alkalinity of a solution. It is measured on a scale of 0 to 14. When a solution is neither acid nor alkaline, it has a neutral pH of 7.0. The more lower than 7.0 the pH is, the more acidic the solution, the more higher than 7.0 the pH, the more alkaline the solution.

Blood is normally slightly alkaline with a pH range of 7.35 to 7.45. The constancy of the blood pH is fundamental to the body's ability to maintain a relatively unchanging internal environment. Its importance is illustrated by the fact that an individual cannot live if the blood's pH goes below 7.0 or above 8.0. For example, blood with a pH of 6.95, which is only slightly acidic, can lead to coma and death.

There is another source of confusion – the logarithm. To understand the logarithm, think of "power." The letters pH can also stand for "power of hydrogen" and the numerical value is defined as the negative base 10 logarithm of the molar concentration of hydrogen ions.

$$pH = -\log10[H+]$$

To simplify, because the medical knowledge is unusual and does not mean the same as mathematic knowledge, we need to know that the pH scale is the difference in **1** between two measurements of pH meaning **10** times more or less, difference in **2** means **100** times, difference in **3** means **1000** times, difference in **4** means **10000** times distinction, etc.

c. Acidity vs. Alkalinity

It is well known that the body's main regulators of acid-alkaline balance are the lungs, liver and kidneys, which are responsible for excreting and metabolizing acids. In acid-alkaline disturbances, there is an imbalance between the quantity of acids produced and the body's ability to respond.

Body acids are formed as end products of cellular metabolism. The average person generates from 50 to 100 mEq acid/day from metabolism of protein, carbohydrates, and fats, and from the loss of alkaline substances in the stools. To maintain a normal pH, an equal amount of acid therefore must be neutralized or excreted. The lungs, kidneys, blood, bones, liver, gallbladder, stomach and pancreas are involved in the regulation of the body’s acid-alkaline balance. Many body functions are designed to regulate acid-alkaline balance including respiration, excretion, digestion, circulation and cellular metabolism.

The acid-alkaline regulation systems are interrelated and work together not to admit acute or chronic changes in the body’s acid-alkaline balance.

The acid–alkaline balance is an important factor in the health and functioning of the body. Optimal health depends on the body's ability to maintain a slightly alkaline state

What causes the body to be acidic? The main factors are:

> Producing too many acidic substances by body's own cells

> Producing too many acidic substances by microorganisms inside the body

> Consumption of acidifying food

> Acute or chronic toxicity of the acid producing compounds (alcohol, chemicals, heavy metals, some medications, etc)

> Low or improper function of the lungs, kidneys, liver and GI organ as well as poor microcirculation and dehydration

> Low capacity of the blood buffer systems, especially bicarbonate buffer, etc

End products of body metabolism mostly are acids. The human being has a complicated, multifunctional mechanism to either neutralize these acids or remove them from the body via (CO2) carbon dioxide, a gas that is eliminated by the lungs or, by keeping (HCO3) - bicarbonate in the blood by the kidneys. The lungs and kidneys are the major organs that help control the blood concentrations of CO2 and bicarbonate ion - HCO3-, and thus help control the pH of the blood.

Removing CO2 from the blood via the lungs or keeping HCO3- in the blood help to increase the pH. This is the alkalizing effect. HCO3- is the alkaline reserve of the body.

Removing HCO3- from the blood via the kidneys lowers the pH. This is the acidifying effect. These processes are the main regulators of pH stability in the blood.

d. Buffers

In the bloodstream, there are substances known as buffers that act chemically to resist changes in pH. The major buffer system in the blood is the CO2-bicarbonate buffer system (shortly "bicarbonate buffer"). It is the most important blood buffer for metabolic acids.

lung↕**CO2 + H2O <==> H2CO3 <==> H+ + HCO3-** ↕kidney

The formation of bicarbonate ions, (HCO3-) takes place by the following reactions:

Hydration of CO2: **CO2 + HOH => H2CO3-**

Dissociation of H2CO3: **H2CO3 => H+ + HCO3-**

The H2CO3/HCO3- combination acts as the primary buffer of the blood.

The bicarbonate buffering system is important in many different cellular processes. Just a few are listed below:

- It is one of the major buffering systems used to maintain the pH of human blood
- It is used to protect the lumen on the stomach during the formation of hydrochloric acid
- It is used to neutralize the pH of the chyme leaving the stomach and entering the small intestine
- This is the main factor of alkalinity of pancreatic juice and bile

The pancreas and liver are alkaline glands because they produce pancreatic juice and bile, which are normally alkaline solutions

Pancreatic juice has pH 7.1- 8.2, and the pH of liver bile is 7.5- 8.8. [82] Thus, the pancreas, liver, and gallbladder are the organs, which are strongly involved in the body's acid – alkaline balance. On the other hand, acidity – metabolic acidosis, changes the bile and pancreatic pH in a harmful way causing serious problems for digestion and for the entire GI tract.

Between all these pancreatic deficiencies, when acidity depletes the alkaline reserve in the body, this process destroys the function of the liver, gallbladder and pancreas. As was mentioned before, those organs are alkaline - they produce alkaline bile and alkaline pancreatic juice. To make them alkaline, the liver and, especially, the pancreas, take the minerals and bicarbonates from the blood. The pH of blood is constant and the body struggles to keep it constant to save the brain, lungs and the heart, which completely shut down if the pH in the blood drops even slightly.

During acidity, the organism chooses the wise strategy for surviving to save the vital organs, such as the heart, lungs, and brain at the expenses of peripheral, "less essential" organs and tissues.

Who first would suffer from over acidity in the body? The liver, gallbladder, and pancreas are the first organs to suffer. In this situation, their ability to take minerals and especially bicarbonates from blood is poor, thus, the pH of their secretion drops (acidic pancreas and bile) and the biochemistry, composition and function of these organs change badly.

e. The Importance of Bicarbonate

Bicarbonate content is a prime factor of alkalinity in bile and pancreatic juice.

Content of Bicarbonate (mEq/Liter) in the human plasma, pancreatic juice and bile.[60]

Body's Fluid --------Bicarbonate

Blood (plasma) ---------- **27**

Pancreatic Juice ------- **92 - 145**

Bile---------- **45**

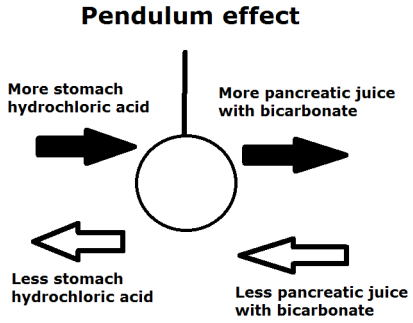
As can be seen in the bile and especially in pancreatic juice, there is much more bicarbonate than in the blood plasma.

Bicarbonate is the main component, which gives pancreatic juice its alkaline property

According to the scientific literature[100, 102, 171], the pancreatic bicarbonate output is strongly related to duodenum pH and regulated by interaction of digestive hormones such as secretin and cholecystokinine with the nervous system. In the presence of fat or protein, digestion products from the stomach, lower the duodenal pH even slightly below 4.5. This leads to near maximum increases in water and bicarbonate secretion. These digestive products in the chyme are equally effective at stimulating pancreatic digestive enzymes secretion, as well.[101]

Connection between gastric secretion of the hydrochloric acid and secretion of the pancreatic juice with bicarbonate is a well known fact. The pancreas is like a stomach working in reverse. It can be described as "pendulum effect" (see picture).

The more stomach acid, the more pancreatic juice with bicarbonate and enzymes is secreted and the less stomach acid, the less pancreatic juice with bicarbonate and enzymes is released.



Bicarbonate in pancreatic juice can originate from two sources; 1) from plasma bicarbonate (80-95%) or 2) from carbon dioxide generated intracellular by the enzyme - carbonic anhydrase. Experiments have shown that the bicarbonate circulating in blood is the main source of bicarbonate in the pancreatic juice.[104]

The scientists found that the pancreas and liver take bicarbonate ions primary from the blood. For example, intravenously injected bicarbonate labeled with the 11C radioisotope appeared promptly in the pancreatic juice. Scratcherd T. and Case R. M. in their work "*The secretion of electrolytes by the pancreas*" in *Am. J. Clinical Nutrition* (1973) and other researchers suggested that pancreatic secretion is directly related to concentration of bicarbonate and experiments

suggested that “most if not all the bicarbonate of pancreatic juice must come from plasma.”[104, 114, 115]

Secretion of bicarbonate increases when the acidic chyme travels from the stomach into the duodenum and then decreases possibly due to the lowering of the amount of bicarbonate capacity inside the pancreas. Infusing bicarbonate into the blood during the digestive process promotes the increasing of bicarbonate in the pancreatic juice.

There is considerable evidence that in the pancreatic disorders there is a decreased amount of bicarbonate in the pancreatic juice and bile.[101, 102]

Saunders J H, Wormsley K G. (1975) pointed out “about defective capacity to secrete bicarbonate in patients with pancreatic exocrine insufficiency, conditions unfavorable to enzymes’ activity (low pH), which may also extend throughout the small intestine”. [100] Talamini G. (2005) also pointed out this connection between duodenal acidity and lower exocrine pancreatic function.[103]

Duodenal acidity mostly depends on a lower quantity of bicarbonate in pancreatic juice and bile. In chronic pancreatitis patients, who very often present pancreatic exocrine insufficiency, duodenal pH may be persistently low.[102,172]

f. Various Research With Bicarbonate

Researches show there is also a direct relationship between bicarbonate concentration and pancreatic juice flow. There is also a positive relationship between the elimination of enzymes and bicarbonate concentrations.[105, 106]

Whitcomb D.C. and Ermentrout D.B. (2004) considered that some toxic harmful environmental factors may cause severe mutations of the genes, such as the cystic fibrosis transmembrane conductance regulator (CFTR), which is a regulated anion channel that is located at the apical (luminal) surface of the duct cell. The pancreas is usually one of the first organs to fail in cystic fibrosis because (CFTR) has such a central role in pancreatic physiology. The pancreatic histology of cystic fibrosis includes all of the features of chronic pancreatitis, as well as scattered ducts that are dilated and filled with protein-rich material that cannot be flushed out of the ducts. New models of pancreatic duct physiology indicate that most bicarbonate secretion is mediated through the CFTR during active bicarbonate secretion rather than through a chloride-bicarbonate antiporter as previously thought.[12, 111]

Professor of Medicine Stephen A. McClave, MD from the University of Louisville School of Medicine, Louisville, KY considered that while healthy people have high bicarbonate concentration in the duodenum, patients with chronic pancreatitis have low bicarbonate

concentration. In this case, acidic fluid builds in the duodenum and inactive enzymes. Pancreatic lipase is inactive if duodenal pH < 4.5.[171]

Giorgio Talamini from the University of Verona, Italy (2005) adds a new potential risk factor for pancreatic cancer after chronic pancreatitis, namely duodenal acidity. Patients with chronic pancreatitis very often present pancreatic exocrine insufficiency combined with a persistently low duodenal pH in the postprandial period. Duodenal acidity may increase the risk of pancreatic cancer in the course of chronic pancreatitis.[172]

Loss of bicarbonate secretion in the pancreatic duct is decreased by chronic systemic metabolic acidosis. Concentration of bicarbonate in pancreatic juice depends on concentration of bicarbonate ions in the plasma.

Metabolic acidosis with low concentration of bicarbonate in the plasma negatively influences pancreatic functions

The relationship between the rate of low pancreatic HCO-3 secretion and high plasma H+-ion concentration was investigated in numerous experiments. A proportional opposite relationship was found between HCO-3 secretion and plasma pH.

Different relationships were found between HCO-3 secretion and plasma HCO-3 concentration during metabolic acidosis. Pancreatic HCO-3 secretion fell to 41% plus-minus 4% of control during acidosis. Plasma H+ - ion concentration, therefore, seems to determine the rate of pancreatic HCO-3 secretion.[173]

J. Nimmo *et al.* (1970) found a lower amount of bicarbonate in the pancreatic juice in the patients with pancreatic disorders by comparison with healthy volunteers.[113]

The importance of plasma bicarbonate is also illustrated by in vivo experiments in which pancreatic secretion was studied under conditions of metabolic acidosis. Canine pancreatic secretion was halved when plasma bicarbonate was lowered to 16 mEq/L[104]

Lieb II, J. and Peter V Draganov, P., from the University of Florida, published the 2008 article, "*Pancreatic function testing: Here to stay for the 21st century*". They considered that decreasing the amount of bicarbonate in the pancreatic juice has a practical clinical importance.

For example, pancreatic function tests especially *the Secretin Stimulation Test* (SST) often has been used to diagnose chronic pancreatitis. During the *Secretin Stimulation Test*, duodenal juice and its volume, pH, and bicarbonate concentration in mEq/L is measured. The damaged pancreas produces decreased volume, bicarbonate, and enzymes in pancreatic juice in response to a

stimulus as compared to the normal pancreas. The bicarbonate output (the product of bicarbonate concentration and volume) is calculated after stimulation by secretin. Standardized ranges are 80-130 mEq/L for the peak bicarbonate. If the peak bicarbonate is less than 80 mEq/L, the patient is very likely to have chronic pancreatitis. The SST, when compared with histology, is 75% sensitive in detecting early stage chronic pancreatitis, and up to 97% for late stage disease with a specificity of 90%. In addition, several histological studies suggest bicarbonate production may be the best way to diagnose early chronic pancreatitis.[116]

g. Trypsinogen Activity

Acidity also promotes premature activation of trypsinogen (inactive enzyme) to trypsin in the pancreatic ducts. Trypsinogen, like all other zymogens, is packaged in zymogen granules, which further retards trypsinogen activation. The high pH (alkaline state) in the duct inhibits activation of the trypsin.[12, 112]

A well-known authority in the pancreatic diseases in the US - Professor David C Whitcomb from Division of Gastroenterology, Hepatology and Nutrition, University of Pittsburgh, USA wrote in 2004[12] about activation of digestive enzymes inside the pancreas:

"Chronic pancreatitis remains a challenging and frustrating clinical problem. In the past few years, however, advances in genetic and immunologic research have spawned new insights and approaches to chronic pancreatitis. Genetic and environmental risk assessment may help identify individuals who are likely to develop severe chronic pancreatitis early in the disease course, and allow targeted attention to reduce confounding risks and slow or prevent this problem in the future. The acinar cells produce large amounts of inactive digestive enzymes (zymogens). Zymogens are flushed from the pancreas in a sodium-bicarbonate-rich fluid that is produced by the duct cells into the intestine, where they are activated. Activation of zymogens while they are still inside the pancreas can be highly destructive, so the exocrine pancreas incorporates redundant protective systems to control the activity of these enzymes. It is when these systems fail that activated digestive enzymes cause direct pancreatic injury and the subsequent immune responses that are recognized as acute pancreatitis. These observations suggest that the key to controlling digestive enzyme activation and pancreatic injury is to control trypsin. The high pH in the duct inhibits activated trypsin by interfering with the transition between trypsinogen and trypsin, and because the ability to flush active enzymes out of the duct may be lost".[12]

The suggestion that the acidifying of the pancreatic juice triggers the premature activation of trypsinogen to trypsin in the pancreatic ducts is not a new one. In 1953 Green NM and Work E., from the Department of Chemical Pathology, University College Hospital Medical School in London, published their article "*Pancreatic Trypsin Inhibitor. 2. Reaction with trypsin*". They determined that the slow rate of reaction between a trypsin inhibitor and trypsin is pH dependent because both proteins have alkaline isoelectric points. The more alkaline the pancreatic juice, the higher the possibility of keeping trypsin inactive within the pancreas. Even neutral pH 7.0 can promote this activation.[190]

Niederau C and Grendellin JH (1988) in the published article in *The Journal of Clinical Investigation,* suggested that acidifying of the pancreatic juice may play a role in the progress of acute pancreatitis.[228]

Scientists from the Department of Internal Medicine, Yale University School of Medicine, New Haven, Connecticut, USA Bhoomagoud M *et al.* (2009) also suggested that metabolic acidosis may be the risk factor for developing pancreatitis. They confirmed experimentally in vivo and in vitro that decreasing pH (acidifiying) increases the sensitivity of the acinar cells to zymogen activation.[229]

h. Flushing inactive pancreatic enzymes prevent their premature activation

Another protective mechanism to prevent premature activation of trypsinogen to trypsin inside the pancreatic duct is quickly sweeping of zymogens out of the pancreas. Flushing and draining pancreatic juice that contains inactive enzymes - zymogens (trypsinogen) to the duodenum as quickly as possible to prevent premature activation of digestive enzymes inside the pancreas is very important in protecting the pancreas from recurrent acute and chronic pancreatitis.

The duct cells line of the pancreatic duct are responsible for fluid and bicarbonate secretion. A high concentration of ions including bicarbonate causes water to enter the lumen by osmosis. Water then flushes the contents of the duct lumen (including zymogens) out of the pancreas into the intestine. Oppositely, low bicarbonate output may lower the amount of water inside the pancreatic ducts. This, in turn, decreases the viscosity of pancreatic juice and slows its elimination.

The Japanese researches Matsuno S, Sasaki Y *et al*. (1991) pointed out that bicarbonate plays the important role in viscosity of pancreatic juice. They found in patients with pancreatitis that bicarbonate secretion and bicarbonate output is decreased and viscosity of pancreatic juice was significantly increased. They also considered that concentrated pancreatic juice may cause the progression of chronic pancreatitis.[102]

i. Acidification of Bile and Bile Refluxes

In normal conditions, alkalinity of bile depends upon the amount of bicarbonate. Low quantities of bicarbonate and subsequently lower pH (*acidity of bile*) cause many harmful changes in the biochemistry of bile.

If the bile becomes more acidic it becomes “aggressive”. Precipitated bile acids and other aggressive components in the *acidic bile* corrode, irritate the bile ducts, gallbladder, pancreatic duct, Sphincter of Oddi, Ampula of Vater and duodenum. This causes spasms, irritation, inflammation, ulcers, etc. Irritations of the mucosa by precipitated bile acids lead to erosion, ulcers and jerky contractions, which disorganize the proper flow of “aggressive” bile/pancreatic juice mix.

“Aggressive” bile often causes reflux - the backflow of bile into the pancreatic duct, or when bile flows upward from the small intestine into the stomach and esophagus. Bile refluxes, which affect the duodenum and stomach, lead to further inflammation, ulcers and cancer.[86]

Bile reflux often accompanies acid reflux, and together they are a formidable team, inflaming the lining of the esophagus and potentially increasing the risk of esophageal cancer.[217, 218, 219]

Billiary pancreatic reflux is when the bile goes back to the pancreatic duct and may initiate acute pancreatitis and provoke the exacerbations in the case of chronic pancreatitis.

Acidic bile is supposed to be a main factor in developing gallbladder stones, which can block the bile and pancreatic ducts causing severe damage to the liver and pancreas.

Regarding Rege RV, Moore EW (1986), the acidification of bile is a main factor in the development of gallbladder stones, which have been documented as blocking the bile and pancreatic ducts and causing severe damage to the liver and the pancreas.[191]

j. The Antimicrobial Activity of Pancreatic Juice

When the pH of pancreatic juice drops below 7.0 the antimicrobial activity is diminished. Rubinstein E *et al.* (1985) found that the antibacterial activity of pancreatic juice was pH dependent. [149] Experiments on people with fistulas of the pancreas showed that in healthy conditions, pancreatic juice is almost sterile. Pancreatic juice destroys almost the whole spectrum of microorganisms.

There are very few microorganisms in the small intestine because intestinal microbial homeostasis is controlled by a variety of factors. Between some of them, pancreatic juice plays a fundamental role in keeping the number of microbes in the small intestine low. There is evidence that the antibacterial function of pancreatic juice is very sensitive to pH, having an optimal activity at pH 8.5 (alkaline condition) and with complete cessation of action at pH 7.0 (neutral reaction of solution).[148]

French researchers Ramare F *et al.* (1993) [150] found similarity between antibacterial factors in the pancreatic juice with trypsin. In other experiments that were conducted by Pierzynowski SG *et al*. (1999), starvation of 48 hours causes a drop in the rate of secretion as well as in the antibacterial potency of the pancreatic juice.[148]

Decreasing pancreatic secretion and acidifying of the pancreatic juice makes the pancreas more vulnerable to infection. Therefore, the restoration of the alkalinity in the pancreas is important for the treatment and prevention of pancreatitis. Alkalinity of the pancreatic juice promotes its antibacterial activity against infection and suppresses the premature activation of trypsinogen to trypsin inside the pancreas, thus promoting self-digestion.

European doctors, who have treated pancreatic disorders at healthy mineral spas for years have considered that the restoration of the normal, slightly alkaline acid – alkaline balance in the body can be a useful therapeutic tool for people with chronic pancreatitis.

k. What Happens to the Pancreas if the Blood Becomes Acidic?

Acidifying of the blood means that pancreatic cells cannot obtain the proper amounts of minerals and bicarbonates from blood to produce normal alkaline pancreatic juice. It leads to a dangerous lowering of the pH of the pancreatic juices, or *acidic pancreas*.

Acidifying of the pancreatic juices can cause many pancreatic problems including:

- Diminishing the activity of the pancreatic enzymes in the duodenum, which cause indigestion. Digestive pancreatic enzymes work only in an alkaline environment

- Reducing the activity of protease inhibitors. If the suppressing activity goes down, than the protease (enzyme that digests protein) is getting active inside the pancreas. The protease starts to digest its own pancreas causing inflammation – pancreatitis

- Precipitation of "aggressive" bile acids, which irritate the bile duct, Ampula of Vater, Sphincter of Oddi, duodenum end eventually the pancreas. This, in turn, leads to bile refluxes when the "aggressive" bile can reach the pancreatic duct, stomach and even the esophagus. Bile/pancreas reflux causes activation of digestive enzymes inside the pancreas, thus inflammation – pancreatitis. Bile/stomach reflux causes inflammation of the stomach, which is called gastritis, stomach ulcers or even cancer

- Precipitation of calcium inside the pancreatic duct leads to stones, which irritate or obstruct the pancreatic duct, causing inflammation – pancreatitis

- Precipitation of calcium inside the gallbladder results in stone manufacturing and blockage of the Sphincter of Oddi. This, in turn, increases pressure inside the pancreatic duct, activates enzymes within the pancreas, causing self-digestion and pancreatitis

-Decreasing of anti bacterial activity of pancreatic juice leads to Candida-yeast overgrowth and Small Intestine Bacterial Overgrowth

- Decreasing viscosity of pancreatic juice with possible slow moving of this fluid to its way to the duodenum. This may cause premature activation of digestive pancreatic enzymes inside the pancreatic duct, thus inflammation – pancreatitis

- Spasms of the Sphincter of Oddi cause back up flow and increases pressure inside the pancreas, causing inflammation – pancreatitis.

Focus on acid – alkaline balance can be an important key in preventing and treating either digestive or hormonal pancreatic disorders

Our ancestors were exposed to totally different foods and ways of eating. Since the agricultural revolution 10,000 years ago, industrial revolution 200 years ago and food revolution 60 years ago, most people have been eating and drinking very different. As a result our digestive system, which is left genetically unchanged, overworks in an unusual harmful manner, thus it is easy vulnerable to many gastrointestinal disorders and diseases.

Metabolic acidosis is more widespread in our society today. Primarily, this happened due to the Standard American Diet.[49, 63] Most of what we eat now is acidic in nature and, therefore, changes the balance toward metabolic acidosis. [88] Many publications focus on prevalence of metabolic acidosis in modern men. [49, 62, 63]

Researchers from the University of California published in a 2002 *American Journal of Clinical Nutrition*, that most health problems stem from the deficiency of bicarbonate in today's food compared to food of our ancestors. Sebastian A., Frassetto L.A. *et al*. (2002), suggested that "diet-induced metabolic acidosis and its sequel in humans eating contemporary diets reflect a mismatch between the nutrient composition of the diet and genetically determined nutritional requirements for optimal systemic acid-base status".[64]

Other researchers proved that modern nutrition produces a low-grade metabolic acidosis in otherwise healthy people. Some studies found that this metabolic acidosis increases with age. [49, 62, 63, 64, 180, 181, 187, 229, 259]

Putting into account that metabolic acidosis harmfully affects the function of the pancreas, correcting and normalizing the body's acid – alkaline balance is very important for preventing and treating all pancreatic disorders and as a result, most of the GI problems. Acidity kills the pancreas!

Interesting facts at a glance:

pH measures the degree of acidity or alkalinity of a solution

Pure water is neutral and has pH of 7.0. Moving outward from 7, a lower pH number equals a more acidic solution and a higher pH number signifies a more alkaline solution

It is important to remember that when acidity increases, the pH decreases

The human body keeps a constant slightly alkaline pH 7.4 acid – alkaline balance in the blood

To maintain alkalinity, the pancreas and liver (bile) take bicarbonate and minerals from blood plasma

In the case of whole body acidity (metabolic acidosis), the pancreas and liver cannot obtain enough alkaline minerals and bicarbonate. We call this condition "acidic pancreas and bile"

There is considerable evidence showing that a primary cause of many pancreatic disorders is a decreasing amount of bicarbonate in the pancreatic juice and bile

In mostly all GI diseases and disorders, to improve the function of the pancreas one needs to normalize the acid – alkaline balance

Acidity of the bile and the pancreatic juice diminishes the activity of pancreatic enzymes in the duodenum, causing indigestion. Indigestion occurs because digestive pancreatic enzymes can only work in an optimally alkaline environment

Acidity leads to the reduction in the activity of protease inhibitors. When protease inhibitors stop working, tripsinogen (inactive enzyme) is converted to trypsin (protease) inside the pancreas causing self-digestion. The protease starts to digest the pancreas causing inflammation and pancreatitis

Acidity leads to the precipitation of "aggressive" bile acids, which irritate the bile duct, Ampula of Vater, Sphincter of Oddi, duodenum, and eventually the pancreas. This irritation, in turn, leads to bile reflux where the "aggressive" bile can reach the pancreatic duct, stomach, and even the esophagus

Bile/pancreas reflux causes the activation of digestive enzymes inside the pancreas, thus causing inflammation and pancreatitis. Bile/stomach reflux causes inflammation of the stomach, called gastritis, which can lead to stomach ulcers or even cancer

Acidity leads to the precipitation of calcium inside the pancreatic duct, resulting in the formation of stones, which irritate or obstruct the duct, causing inflammation and pancreatitis

Acidity leads to the diminishing of the anti-bacterial activity of pancreatic juice. Due to less anti-bacterial activity, Candida-yeast overgrowth and Small Intestine Bacterial Overgrowth are developed

Acidity leads to a lowering in the viscosity of the pancreatic juices, which slows the movement of the pancreatic juice. Slow-moving pancreatic juice may cause the premature activation of digestive pancreatic enzymes inside the pancreatic duct, thus causing inflammation and pancreatitis

Acidity leads to the irritation and spasm of the Sphincter of Oddi and subsequently backs up the flow of digestive juices into the pancreas, increasing the pressure inside the pancreas, causing inflammation and pancreatitis

Acidity leads to production of the gallbladder stones, which can block the Sphincter of Oddi, increase pressure inside the pancreatic duct and cause premature activation of the enzymes within the pancreas, thus leading to self-digestion

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Chapter 5-Pancreas, Liver, and Bile: Counterparts or Huge Enemies?

For individuals lacking a medical background

In the human body, the pancreas and bile can be figuratively in good or very bad relationships. In a healthy situation, they can be friends, but in an unhealthy situation, they can infect one another, causing diseases. For example, gallbladder stones or pancreatic cancer both can form blockages of bile that cause huge problems for the liver and the pancreas.

Anatomy and Physiology

To truly appreciate the relationship between the liver and the pancreas, one needs to understand the anatomy and physiology of these organs.

The liver is our body's chemical factory and performs many vital tasks. Everything we eat and digest makes its way to the liver, and the liver uses the food materials to produce vital nutrients for our cells, as well as for our whole body. The liver's most important functions are manufacturing and releasing bile and removing the toxins from our body by dividing them into water-soluble and fat-soluble wastes.

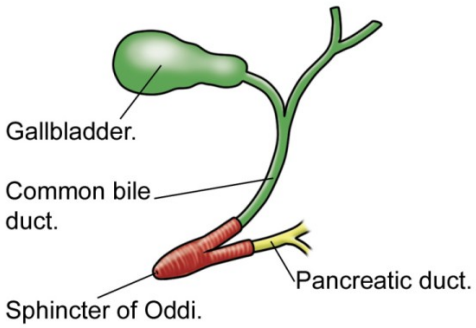
First, the liver produces water-soluble wastes. Then it makes these wastes less toxic and transports them to the blood and the kidneys for elimination from the body.

Second, the liver moves the fat-soluble wastes into the bile before moving the wastes through the small and large intestines and out of the body. Bile serves to eliminate a variety of toxic substances from the body. These substances include the products of the body's metabolism such as cholesterol and bile pigments, as well as some toxic chemicals, drugs and heavy metals.

The cells of the liver secrete bile into a network of ducts. These ducts meet to form the common bile duct, which carries bile from the gallbladder and liver.

The common bile duct merges with the pancreatic duct. The pancreatic duct carries the pancreatic juice with digestive enzymes from the pancreas into a small cavity (the Ampulla of Vater) that opens into the duodenum, the first section of the small intestine.

It is very important that the pressure in the pancreatic duct is always higher than the pressure in the bile duct; therefore bile cannot reach the pancreatic cells. The mixture of bile and the pancreatic juice goes through the Ampulla of Vater into the duodenum.



Around the common bile duct, pancreatic duct and the duodenum wall there is a muscle valve called the Sphincter of Oddi. The Sphincter of Oddi controls secretions from the liver, pancreas, and gallbladder into the duodenum. Spasm or blockage of this muscle valve may cause pancreatic juice to back up, thereby increasing the pressure inside the pancreatic duct. Digestive enzymes trapped inside the pancreas start to digest their own pancreatic cells, causing congestion, inflammation, pain, cysts and finally the death of pancreatic tissue.

Hepatitis, fatty liver, Candida-yeast overgrowth, parasites, congestion, inflammation, infection, body's acidity levels and poor eating habits can cause the bile to be thick and acidic, and make it difficult for the bile to move through the ducts. Those factors can lead to gallbladder stones, which may block bile movement, increasing the pressure into the Ampulla of Vater and backing up the pancreatic juices.

When the bile becomes acidic it also becomes very aggressive. This means that aggressive bile irritates and corrodes the walls of the ducts, causing a condition known as biliary (bile) reflux. This causes spasms of the Sphincter of Oddi and the pancreatic and common bile ducts. This is very dangerous because instead of the toxic acidic bile going to the duodenum, the toxic acidic bile travels into the pancreas, which activates the pancreatic digestive enzymes. Thus, pancreatitis begins.

Additionally, when the acidic, aggressive, toxic bile is pushed out into the duodenum, it erodes and irritates the gut's walls causing the duodenal ulcers. This aggressive bile causes the duodenum walls to contract in a jerky motion that pushes the bile up inside the stomach or even esophagus. Thus, stomach and esophagus inflammation, ulcers and possibly cancer may develop.

For individuals with a medical background

To understand complex expressions, we will use the following medical words:

A. ***bile***, ***gall*** *or* ***chole*** (***biliary*** is the connection to the **bile** or to the **gall bladder**)

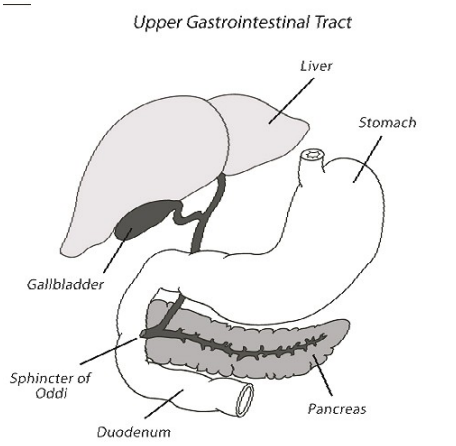
B. ***Cholecyst*** (***chole*****)** is bile; ***cyst***- is the bladder or sac)

C. ***Cholecystectomy*** refers to the removal of the gallbladder

To understand the liver, bile and the pancreas connection, we have to accept the idea that all of the upper gastrointestinal (GI) tract organs such as the stomach, liver, gallbladder, pancreas and duodenum work together as an orchestra. Failure in any one of these organs will cause problems to the whole GI system. Digestive hormones and the nervous system conduct this GI tract orchestra. The upper GI tract is regulated by the nervous system and special blood messengers (digestive hormones) and thus, works as an entire system.

Bile is not a gastrointestinal organ, but this fluid has a remarkable impact on digestion and particularly on pancreatic health. That is why authors will use often this connection between pancreas and bile.

a. Anatomy and Physiology



Chewed food travels into the stomach where the hydrochloric acid and pepsin (stomach enzyme) begin digestion, mostly of proteins. Semi digested acidic food, which is called "chyme" goes into the duodenum, the first section of the small intestine.

Digestive hormones cholecystokinin and secretin are released into the blood and bind to receptors on the pancreatic acinar and ductal cells, ordering them to secrete large quantities of digestive enzymes, water, and bicarbonate.

Cholecystokinin: The name of this digestive hormone describes its effect on the biliary system. *Cholecysto* = gallbladder and *kinin* = movement. The most potent stimulus for release of cholecystokinin is the presence of fat in the duodenum. Once released, it also stimulates contractions of the gallbladder and common bile duct, resulting in delivery of bile into the duodenum.

Secretin: This hormone is secreted in response to acid in the duodenum. Its effect on the biliary system is very similar to what was seen in the pancreas. It stimulates the biliary duct cells to secrete bicarbonate and water, which expands the volume of bile and increases its flow out into the intestine. Any time the duodenal pH drops below the 4.0-5.0 range, secretin is released, resulting in the release of bicarbonate and water in the pancreatic juice.

Bile is produced in the liver. The human liver produces about a quart of bile per day. When food is released by the stomach into the duodenum in the form of the acidic chyme, the duodenum releases cholecystokinin and secretin, which cause the gallbladder to release the concentrated bile to complete digestion.

Common bile ducts, which carry the bile from the liver and gallbladder, have a close anatomical connection with the pancreatic duct. They merge with each other making a chamber known as the Ampula of Vater, which is the entrance point to the duodenum. The common bile duct, pancreatic duct and opening to duodenum are covered by a muscle valve known as the Sphincter of Oddi.

If the the Sphincter of Oddi is closed, bile is prevented from draining into the intestine and bile instead flows into the gallbladder, where it is stored and concentrated up to five times its original potency between meals. This concentration occurs through the absorption of water and electrolytes.

b. Bile

The main components of bile are:

- Water
- Cholesterol
- Lecithin (a phospholipid)
- Bile pigments
- Bile salts and bile acids
- Different fat-soluble toxic substances
- Small amounts of copper and other excreted metals
- Bicarbonate and other ions such as sodium, potassium, magnesium, chloride, calcium, etc

Bile has two broad functions: it plays a digestive role in the breakdown and absorption of fat and removes toxic substances from blood, which cannot be eliminated by the kidneys. These toxic substances are usually fat soluble. These toxic substances may be produced internally (such as bile pigments) or externally (such as heavy metals, drugs and other chemicals).

Bile is an active emulsifying (suspension of fats) agent and thus plays a part in the digestion and absorption of fat from the intestine.

Bile Summary

> The liver continually secretes bile

> Approximately 50 - 120 ml of bile may be stored in the gallbladder

> Upon gallbladder contraction, bile passes from the gallbladder to the cystic duct and then to the common bile duct throughout the Sphincter of Oddi and Ampulla of Vater to the duodenum

> Bile is composed of water, bile salts, bile acids, cholesterol, bilirubin, phospholipids, sodium, potassium, chloride, calcium and bicarbonate

> Bile salts cause fat emulsification, thus, helping in fat absorption

> Without bile salts, fat and fat-soluble vitamins (A, D, E, K) are not absorbed

c. Pancreas and Bile Similarities

The pancreas and bile share many similar characteristics including:

1. Both bile and pancreas (pancreatic lipase) are responsible for proper fat digestion. Emulsification is the real key to the proper digestion of fats. The large fat molecule presents comparatively small surfaces for the pancreatic lipase to break up the fat on the small particles, which can be digested in the small intestines. Bile breaks down the large fat parts to tiny droplets (emulsification). Process of emulsification by the action of bile provides lipase with an enormously increased surface to work on

2. Bile and pancreatic juice both have a large amount of minerals and bicarbonates and in normal condition is alkaline, where the pH is more than the 7.0-8.0 range. Fluid alkalinity is essential for neutralizing chyme that is coming from the stomach

3. Both bile and pancreatic juices travel into the duodenum via the bile and pancreatic ducts. They merge with each other before entering the duodenum and the mix of the pancreatic and bile juices (also called “pancreatic-bile secretion”) enter the duodenum through the Sphincter of Oddi

4. Negative altering of the biochemistry of the bile or pancreatic juices can possibly back up these fluids that can lead to both serious and fatal diseases

5. Working hard to produce both 1.0 -2.0 liters of bile or pancreatic juice, the liver and pancreas depend on the proper supply of water, proteins, vitamins, minerals, trace elements and bicarbonate. The lesser amount or lack of these vital nutrients will change the quality, quantity and biochemistry of the bile and pancreatic juice, making them acidic (decreasing their pH), which, in turn, can cause many liver, gallbladder and pancreatic disorders

6. Liver and pancreatic cells produce protein more than other cells of the body

7. The pancreas and liver are also vulnerable to the internal and external toxic environments, which are caused by chemicals, alcohol, microorganisms, parasites, inflammation, immune or metabolic disorders, age, dysbiosis – Candida-yeast overgrowth and Small Intestine Bacterial Overgrowth, hereditary disorders, etc

d. Pancreas and Bile Antagonistic Relationship

The Pancreas and bile begin a hostile relationship mostly when the pancreatic juice and bile become acidic

Let us focus on why the bile becomes acidic, thus, making bile more aggressive to mucous walls. Usually these two processes come together and the big player in this process is the low pH of bile, referred to as *acidic bile*.

In a healthy individual, the alkaline bile from the liver or from the gallbladder (pH 6.2-8.5) and alkaline pancreatic juices (pH 7.1-8.2) [82] flood the duodenum shortly after acidic chyme passes through from the stomach into the duodenum. These highly alkaline fluids neutralize the acidic chyme and raise the pH in the duodenum up to alkaline levels, allowing the perfect environment for this stage of digestion.

Pancreatic enzymes can only function optimally in a pH above 7.0

Optimum pH for pancreatic lipase activity is 8.0 and for trypsin 7.8 - 8.7 [170] As long as the body is able to do this, proper digestion will occur.

e. The vital components of bile are bile acids and bile salts

The function of these remarkable molecules is inextricably involved with cholesterol. The two main bile acids, cholic acid and chenodeoxycholic acid, are both made from cholesterol in the liver and pass into the bile in combination with amino acids (glycine conjugates and taurine conjugates), as bile salts.

Cholesterol is virtually insoluble in water, so the body has developed a special strategy to excrete this substance. Cholesterol excreted by the liver is partly extracted from the blood and partly produced by the liver itself. The body uses bile salts as a vehicle for cholesterol and other fat-soluble substances. The bile salts are the molecules, which have a water-soluble (*hydrophilic*) side and a fat-soluble (*hydrophobic*) side.

This allows bile salts to make small parcels (‘micelles’) including several different molecules, with cholesterol as contents and bile salts as the wrapping. The hydrophobic aspect of the bile salt faces inwards, and the hydrophilic aspect faces outwards into the aqueous component of bile.

The bile micelles pass into the duodenum, where the detergent action of the bile salts emulsifies fats, which are then broken down by the pancreatic lipase. Bile salts also assist the absorption of the end products of fat digestion. Both bile and lipase are necessary for the proper absorption of fats in the small intestine. Without proper quality and quantity of bile and pancreatic lipase, there is deficiency of the vital fat-soluble vitamins, A, D, E and K, and malabsorption causes fat to appear in the fecal mass (steatorrhoea).

The bile salts travel into the small intestine where they assist in the emulsification of dietary lipids, promote the absorption of fat soluble vitamins, and allow the fecal excretion of excess cholesterol.

It is clear that bile acids are the acidic component of bile. Bile salts are neutral and bile salts in combination with bicarbonate are the alkaline component of bile. Normally, bile has 12 g/L bile salts and bile acids with a ratio of 99.08% bile salts (glycine conjugates - 75%, taurine conjugates – 24.8%) and free bile acids only 0.2%.[76]

A deficiency of electrolytes and bicarbonates in the body causes deficiencies of them in the bile and leads to changing the bile pH to less than 7.0. Thus, the ratio between bile acids and bile salts changes by increasing the bile acids in the bile.

Acidity of bile is a key for many gastrointestinal troubles

When acidic chyme passes into the duodenum and when the bile has turned acidic, then acidic milieu is formed. Digestive pancreatic enzymes cannot function properly in an acidic environment. If the partially digested food from the stomach is unable to be fully alkalized in the duodenum, then the digestive enzymes don't work and digestion is greatly inhibited.

Acidification of bile can cause precipitation of aggressive bile acids. W J Fitzpatrick, *et al.* (1986) found that 50% of the bile acids were precipitated at pH less than 5.0, compared with only 26% at pH greater than 6.0. [75]

After bile acidifies and the body is unable to correct this acidification, instead of bile salt more bile acids are present in the bile. Bile acids are very aggressive substances and they irritate and burn surrounding cells, ducts and intestinal mucosa. This, in turn, causes spasms, burns, inflammation, and even cancer. Irritated tissue aspires to get rid of aggressive bile causing bile reflux; the wrong way traffic for bile. When aggressive acidic bile comes to the duodenum, ulcers and inflammation occur. Three-fourths of ulcers are duodenal ulcers. Why do ulcers generally occur in the duodenum, rather than in the stomach? Because the pushed out concentrated aggressive bile can cause more damage in the duodenum.

When acidic, aggressive, toxic bile goes into the stomach and even esophagus, it leads to heartburn, stomach inflammation, gastritis, gastric ulcers, and cancer.[86]

Anderson MC *et al.* (1979) found the pancreatic – bile reflux, when the active digestive pancreatic enzymes enter the bile duct and cause damage and inflammation to the bile duct or even gallbladder.[85]

The worst possible scenario occurs when wrong way traffic brings bile into the pancreatic duct. It is a well-known fact that even a small amount of bile in the pancreatic duct causes pancreatitis, as Yamada T. *et al.* (1999) wrote in their *Textbook of Gastroenterology*.[81]

Interesting facts at a glance:

The liver removes the toxins from our body via bile

Bile has two broad functions: it plays a digestive role in the breakdown and absorption of fat, and through the bile, removes toxic substances from blood

The common bile duct merges with the pancreatic duct

A blend of bile and pancreatic juice goes through the Ampulla of Vater into the duodenum

Around the common bile and pancreatic ducts is a muscle valve called the Sphincter of Oddi

Spasm or blockage of the Sphincter of Oddi may cause pancreatic juice to back up, activation of pancreatic enzymes, thus causing congestion, inflammation, pain, and finally the death of pancreatic tissue

Bile normally is alkaline; when the bile becomes acidic it also becomes very aggressive

Acidic bile irritates and corrodes the walls of the ducts and gut causing "wrong way traffic": bile- refluxes

Bile-refluxes may cause pancreatitis, duodenal and stomach ulcers

In a healthy person, the alkaline bile and alkaline pancreatic juice neutralize the acidic chyme, which comes from the stomach, and raise the pH in the duodenum up to alkaline levels, allowing the perfect environment for pancreatic digestive enzymes to work

Acidity of bile and pancreatic juice is a provocative factor for many gastrointestinal troubles

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Chapter 6-Development of Pancreatic Disorders

For individuals lacking a medical background

To understand how the pancreas works, it would be easy to compare it with a large multifunctional manufacturing company. To function effectively, both the pancreas and company require good management, working plants, and efficient supply of labor.

Everybody knows, that if the boss is crazy or confused, the management is poor and hysterical, or if the computers shut down then this company will fail.

Continuing with our analogy, all manufacturing companies require the room and space for a conveyer belt or assembly lines.

The pancreas has a very complicated structure with different kinds of pancreatic cells, acinar cells, islets of Langerhans, small and big ducts, valves and gates. Different cells produce different substances. Some substances travel into the blood and other substances travel to the small intestine.

To manufacture the pancreatic juice and hormones, the pancreas needs to be supplied with water, protein, minerals, bicarbonate, and other nutrients, as well.

To summarize, the pancreas needs proper regulation, normal structure, function, and eventually an efficient supply of workers.

Pancreas work is regulated by the central and autonomic nervous systems.

If we taste, smell, touch, listen, see, and even think about food, our brain will send the signal to the pancreas: “Hey, be ready to work, some food is coming”. A number of nervous stimuli travel to the pancreas through the peripheral nervous systems. Like Pavlov’s salivating dogs reacting to the dinner bell, the pancreas is affected and activated by our senses.

Another way the pancreas can be regulated is by the blood. The stomach, duodenum and pancreas release many digestive hormones – blood messengers. These digestive hormones travel to the stomach, liver, gallbladder, Sphincter of Oddi and the duodenum with very important messages: “Please, work together collectively to properly digest the eaten food.”

Partially digested food (chyme) moving from the stomach to the duodenum (beginning of the small intestine) activates the formation of digestive hormones, such as secretin and cholecystokinin. The bloodstream carries these hormones to the pancreas, liver and gallbladder. The function of secretin and cholecystokinin is to carry information regarding the amount of undigested proteins, carbohydrates and fats that are in the partially digested food, as well as the amount of bicarbonate that is needed to neutralize the acid from the stomach. The healthy pancreas then provides the exact amount of its own bicarbonate and digestive enzymes needed to finish the job.

There is a large and complicated digestive conveyer for food. All eaten food is mashed, mixed with water (digestive juices) and digested to the small particles, which can easily go through the

gut walls into the blood and then to the living cells of our body. The pancreas is a main member of the "digestion team" because of its vital task – producing digestive enzymes. We can eat very healthy and nutritious food, but, if the food cannot be properly digested and travel to our cells, we will die from starvation.

Many pancreatic diseases are developed because of the improper structure and function of the pancreas. These diseases very rarely start by suddenly falling out of the sky. Usually, the diseases start from vague symptoms such as gas, bloating, cramps, and discomfort in the upper stomach, craving, constipation, diarrhea, weight gain or loss, etc.

Fatigue, allergies and chronic infections due to low immunity, deficiencies of some vitamins and minerals, mental and emotional problems, wounds, and traumas may have a direct connection with improper pancreatic functions.

To make it very simple, can you imagine an individual who is forced to work hard, overtime, under stress and doesn't have enough nutritional food? This person eventually will be overwhelmed, exhausted, sick and tired and doesn't have a choice for a long life. So is the same with our pancreas.

The modern population eats processed "dead" food without living natural enzymes. The lack of living enzymes forces the pancreas to work hard and produce more of its own digestive enzymes to digest food.

The modern population is mostly acidic and has a deficiency of bicarbonate, potassium, magnesium, zinc, cobalt, and other minerals and has a low intake of vitamins. Without these vital nutrients, the pancreas cannot work properly.

Stress kills us our pancreas by harshly disorganizing its hormonal and neural regulations.

The modern population eats various food combinations, which are impossible in nature. These combinations are very difficult to digest, thus, the pancreas needs a long and difficult time to work.

It is of no wonder that if the pancreas, as the main digestive organ, is sick, that so many modern individuals suffer from digestive disorders.

For individuals with a medical background

Today, medical practitioners have a different point of view on the cause, development and possible treatment of pancreatic disorders according to their own specialties and experience. However, successful treatment of pancreatic diseases is commonly difficult and requires different methods and approaches to achieve the result. Because the pancreas is a very complicated essential organ with many puzzles and mysteries, prevention and treatment of pancreatic disorders are not easy tasks.

If the pancreas is compared to a large multifunctional modern chemical company, the pancreas needs:

a. Well-organized regulation

b. Normal working structure and function

c. Efficient supply of water, minerals, trace elements, bicarbonates, and vitamins

a. Well-Organized Regulation

The nervous system and digestive hormones regulate the pancreas. When a meal is ingested, hormones such as Gastrin, Vasoactive Intestinal Peptide (VIP), Gastric Inhibitory Peptide (GIP), Secretin, Cholecystokinin (CCK), Encephalins and other digestive hormones and neurotransmitters stimulate pancreatic enzymatic release into the pancreatic duct.

Nervous System Regulation

The central nervous system (CNS) is the headquarters that regulates our common behavior for survival and sends commands to our inner organs. Therefore, the central nervous system signals the pancreas to manufacture the necessary digestive enzymes.

Famous Russian physiologist Ivan Pavlov proved the important role of CNS in digestion. He performed classical experiments with salivating dogs that reacted to the dinner bell. He also demonstrated how the CNS regulates pancreatic secretion. The pancreas is affected and activated by what we see, hear, smell and touch (with our tongues). The neurotransmitter serotonin, that controls brain function, is also a main regulator of the functioning of the gastrointestinal tract.

Additionally, the Autonomic Nervous System (ANS) regulates the relationship between the digestive organs and glands such as the stomach, pancreas, duodenum, liver, gallbladder and colon. Many factors influence nervous system regulation of normal pancreatic work, including:

- Stress (mental, physical, chemical, and so on)
- Age
- Some pharmaceutical drugs
- Post-surgery conditions such as gastroectomy, cholecystectomy, partial pancreatectomy, etc.
- Alcohol, tobacco, caffeine and recreation drugs
- Disorders of the nervous system
- “Eating on the go” and distraction during eating (TV, books, game, etc.).
- Irregular eating habits and dieting

- Depression, anxiety and neurosis
- Toxic substances inside and outside the body
- Fasting and harsh “liver flush”

Hormone Regulation

Partially digested food (chyme) moving from the stomach to the duodenum causes the formation and releasing of some digestive hormones: secretin, cholecystokinin (CCK), Gastric Inhibitory Peptide (GIP), Vasoactive Intestinal Peptide (VIP), etc. These digestive hormones are blood messengers that travel via the bloodstream to the pancreas, liver and gallbladder. These hormones send the simultaneous commands for the proper communication of these organs. Secretin and cholecystokinin carry information regarding the amount of undigested proteins, carbohydrates and fats in the partially digested food, the quantity of digestive enzymes the pancreas needs to release and how much bicarbonate is needed to neutralize the acid from the stomach.

There are two main types of exocrine pancreatic secretions: (1) the aqueous alkaline type, which is rich in bicarbonate ions, and (2) the enzyme rich type.

Secretion Producing Cells Messengers

For bicarbonate ions duct cells is Secretin

For digestive enzymes acinar cells is CCK

Digestive hormones also promote the production and release of bile and regulate the opening of pancreatic and bile duct valves (Sphincter of Oddi). Spasms of these valves cause back up of pancreatic juices, which disrupt normal pancreatic functions.

Secretin is a hormone that is manufactured by special cells in the mucous membrane of the small intestine. Secretin production is stimulated by the acidic chyme from the stomach.

The main actions of Secretin include:

> Stimulating the secretion of pancreatic juice and bile, which are rich in bicarbonate ions

> Enhancing the effects of Cholecystokinin (CCK)

> Increasing the liver to secrete bile

> Inhibiting the production of hydrochloric acid in the stomach

> Promoting growth and maintenance of the pancreas

Stomach Acid => Cells of the Duodenum => Secretin

Secretin => Liver => Bile

Secretin => Pancreas=> Bicarbonate

Cholecystokinin (CCK) is a digestive hormone that is manufactured by special cells in the mucous membrane of the small intestine. CCK production is stimulated by the presence of food in the duodenum.

The main actions of Cholecystokinin (CCK) include:

> Increasing secretion of pancreatic juice rich in digestive enzymes

> Opening the Sphincter of Oddi

> Contracting the gallbladder to deliver bile into the duodenum

> Inhibiting gastric secretion and motility

> Possibly reducing hunger

Food => Cells of the Duodenum => Cholecystokinin (CCK)

Cholecystokinin (CCK) => Gallbladder => Release Bile

Cholecystokinin (CCK) => Liver => Produce Bile

Cholecystokinin (CCK) => Pancreas => Pancreatic Enzymes

Gastric Inhibitory Peptide (GIP) is a hormone that is manufactured by special cells in the mucous membrane of the small intestine. This digestive hormone is released when the chyme entering the small intestine is rich in triglycerides, fatty acids, and glucose.

The main actions of Gastric Inhibitory Peptide (GIP) include:

> Stimulating beta cells to release insulin

> Inhibiting gastric secretion and motility to protect the duodenum from acid damage

> Stimulating lipogenesis (the process that converts excess dietary carbohydrates into fat for storage as a source of long-term energy by adipose tissue)

> Stimulating glucose use by skeletal muscle cells

Vasoactive Intestinal Peptide (VIP) is a hormone that is manufactured by special cells in the mucous membrane of the small intestine. This digestive hormone is released when the chyme enters the small intestine.

The main actions of Vasoactive Intestinal Peptide (VIP) include:

> Stimulating secretion of bicarbonate into pancreatic juice

> Stimulating secretion of water into pancreatic juice and bile

> Inducing smooth muscle relaxation (gallbladder, Sphincter of Oddi, etc.)

> Inhibiting gastric secretion

> Dilating intestinal capillaries

Many factors influence the normal functions of these digestive hormones, including improper food combinations, obesity, alcohol, cigarettes, some medications, processed food, surgeries, etc.

Pancreatic Juice Secretion

The pancreatic juice secretion has the following three different phases:

Cephalic Phase: The word cephalic comes from the Latin word “cephalicus” which means "head". In the cephalic phase, pancreatic juice secretion is stimulated by the vision, smell, taste, sounds, or thoughts of food. The greater the appetite, the more intense are the stimulations. This phase is called cephalic because the central nervous system sends the nerve impulses initiating digestive process. These nerve impulses stimulate branches of the vagus (parasympathetic) nerve, which promotes secretion of gastrin. Gastrin is the digestive hormone manufactured by the stomach mucosa. Gastrin causes the production of stomach acid and initiates secretion of the pancreatic enzymes. The cephalic phase prepares the digestive system to receive food by enhancing pancreatic secretion when the senses are stimulated by appetizing food.

Gastric Phase: During the gastric phase of pancreatic juice secretion, food reaches the stomach. In response to stomach distension, the gastric mucosa releases the digestive hormone gastrin and this, in turn, continues to stimulate pancreatic juice secretion. Distension of the stomach causes vagus nerve stimulation, which results in the release of small amounts of pancreatic juice high in enzyme content.

Intestinal Phase: The intestinal phase of pancreatic juice secretion begins with the arrival of acidic chyme (partially digested food from the stomach) into the duodenum. The acidic chyme stimulates the release of digestive hormones from the mucosa of the small intestine into the blood such as secretin and cholecystokinin (CCK). Secretin stimulates the pancreas to release copious amounts of bicarbonate and water. In response to the presence of fats and partially digested proteins in the duodenum, CCK is released to stimulate the increasing of pancreatic enzyme secretion. Stimulation of the vagus nerve branches enhances the release of enzymes and aqueous components. Activation of sympathetic nerves inhibits pancreatic secretion.

Understanding the mechanisms, which underlay pancreatic juice secretion, helps to realize the factors that may cause pancreatic disease or increase pain when the pancreas is damaged.

b. Normal Structure and Function of the Pancreatic Gland

Many factors influence the normal structure and function of the pancreatic gland including:

- Metabolic acidosis with deficiency of minerals, trace elements and bicarbonates

- Dehydration
- Deficiency of proteins and some vitamins
- Congestion (gallbladder sludge, sand, stones, Sphincter of Oddi dysfunction, scarring of pancreatic ducts, bile reflux, etc.)
- Inflammation (acute or chronic pancreatitis)
- Infection (viral or bacterial infections and parasite infestations)
- Candida-yeast overgrowth, Small Intestine Bacterial Overgrowth (SIBO)
- Trauma or surgery of the liver, gallbladder, and pancreas and some endoscopic procedures
- Cancer
- Alcohol abuse
- Liver disease (hepatitis and cirrhosis)
- Genetic factors (cystic fibrosis, pancreas divisum, etc.)
- Fatty pancreas
- Hypercalcaemia, hyperlipidemia and other factors

Severe body acidity levels, smoking, alcohol, drugs, some medications, Candida-yeast overgrowth, and toxic aggressive bile critically suppress the pancreatic cells from producing the right amount and quality of digestive enzymes.

All of these structure and functional damages rarely develop in one day or even one week. From the beginning, the functional (reversible) pancreatic disorders may cause structural changing of the pancreas. When the pancreatic functional capacity is exhausted, pancreatic failure (almost irreversible) begins. This process usually takes years. That is why, it is essential to change the lifestyle and start the healing procedure even after the first signals and messages the pancreas sends.

c. Efficient Supply of Water, Minerals, Trace Elements, Bicarbonates, and Vitamins

The pancreas produces 1.5 – 2.2 liters of alkaline pancreatic juice daily, which travels into the duodenum through the pancreatic duct. Pancreatic juice contains water, protein, mineral salts, bicarbonate, and enzymes that aid in the digestion of proteins, carbohydrates, and fats. Another important role of the pancreatic juice is neutralizing the acidic chyme.

The pancreatic enzymes work only when the pH of the intestine is slightly alkaline. The food coming from the stomach has been acidified, so the body must provide enough alkalinity for the enzymes to work.

A deficiency of bicarbonate (the major component of pancreatic juice) decreases alkalinity in the duodenum, which, in turn, inhibits the normal function of digestive pancreatic enzymes.

Deficiency of water, proteins, vitamins, minerals, trace elements, and bicarbonates leads to a severe changing in composition of pancreatic juice and decreasing of activity of digestive enzymes. Pancreatic juice contains sodium, potassium, magnesium, calcium, and many trace elements such as zinc, cobalt, selenium, and molybdenum. Most pancreatic enzymatic functions depend on small amounts of essential trace elements. The body cannot synthesize trace elements, therefore, they must be obtained through food, healing mineral water or supplementation.

Abundant digestive enzyme production and their proper elimination are crucial for maintaining optimal health. If the digestive enzymes don't function properly or the pancreas doesn't secrete enough of the enzymes needed for normal digestion, exocrine pancreatic deficiency ensues. When the pancreatic deficiency is severe, malabsorption (impaired absorption of nutrients by the intestines) may result, leading to deficiencies of vital nutrients.

Millions of Americans suffer from a variety of gastro-intestinal disorders including abdominal pain, cramps, gas, bloating, malnutrition, alteration in bowel habits, foul-smelling stool, etc. Many of them have exocrine pancreatic deficiency and don't realize it. Those suffering from this deficiency can eat a healthy diet, but the body will not be able to utilize the nutrients from the food. As a result, their organisms are literally starving.

In addition, without the proper amount of high quality digestive pancreatic enzymes, people suffer from a deficiency of essential minerals, trace elements and vitamins. Individuals are continually tired, develop chronic diseases, and age prematurely. In the worst case scenario, they develop pancreatic cancer.

Many of these problems overlap with each other and can cause the hidden exocrine pancreatic deficiency to completely shut down the body by ceasing the functions of the pancreas.

Smoking, alcohol, drugs, some medications, Candida-yeast overgrowth and toxic "aggressive" bile suppress the pancreatic cells and keep them from producing the needed amount of proper quality digestive enzymes.

Interesting facts at a glance:

Pancreas has a very complicated regulation, function, and structure

Pancreatic work is under control of the central and autonomic nervous systems

The pancreas releases digestive hormones – blood messengers to regulate the digestive process

Secretin and cholecystokinin (CCK) are the most researched digestive hormones

Secretin stimulates secretion of pancreatic juice and bile, which are rich in bicarbonate ions. Cholecystokinin (CCK) increases secretion of pancreatic juice rich in digestive enzymes

Many factors can influence the normal structure and function of the pancreatic gland

Preliminary reversible functional or biochemical disorders later lead to structural nonreversible changes

Severe body acidity, alcohol, smoking, drugs, some medications, Candida-yeast overgrowth and toxic aggressive bile critically suppresses the pancreatic cells from producing the right amount and quality of digestive enzymes

Pancreatic juice contains water, protein, mineral salts, bicarbonate, and enzymes that aid in the digestion of proteins, carbohydrates, and fats

Deficiency of water, proteins, vitamins, minerals, trace elements, and bicarbonates leads to a severe changing in composition of pancreatic juice and decreasing of digestive enzyme activity

Millions of Americans suffer from a variety of gastro-intestinal disorders including abdominal pain, cramps, gas, bloating, malnutrition, alteration in bowel habits, foul-smelling stool, etc. Many of them have exocrine pancreatic deficiency and do not realize it

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Chapter 7-Biotherapy Functional Clinical Classification of Exocrine Pancreatic Disorders

For individuals with a medical background

There are no classifications of pancreatic diseases that may satisfy and unify all specialists. All classifications make sense and are getting practical if they help primary care physicians or medical practitioners to postpone the development of the final stage of the pancreatic diseases, the condition when medical approaches usually are narrowed, and possibilities for treatment are restricted.

Most chronic diseases and disorders, particularly gastrointestinal problems, have three stages of development: functional (reversible), structural (partially reversible), and final (non-reversible) stage. Special medical literature does not have any terms for functional pancreatic disease. Therefore, there are no prevention and treatment options.

Principally, digestive disorders vitally depend upon the proper amount and quality of the pancreatic juice and bile. All digestive diseases have common often-overlapping symptoms such

as low appetite, belching, heartburn, gas, abdominal distention, cramps, abdominal pain, diarrhea, constipation, etc. Nearly all of these symptoms depend on poor digestion of food due to a low amount and quality of pancreatic juice and bile. Evaluation of the common digestive symptoms may show the level of pancreatic deficiency.

It is very difficult to diagnose the first stages of the exocrine pancreatic deficiency by common tests. Using clinical testing, evaluation of the digestive symptoms may assume the percentage of pancreatic involvement, the level of the damage and the stage of the exocrine pancreatic deficiency.

Prevention and treatment of the gastrointestinal disorders is usually focused on the hollow digestive organs such as the stomach and small and large intestines. This focus doesn't really cover the pathogeneses of most diseases and disorders of the GI tract. Clinical tests and autopsy dates suggest that exocrine pancreatic diseases and certainly chronic pancreatitis are more common than previously believed both in diabetic and non-diabetic individuals. Some experts indicate pancreatic involvement in 10% - 13% of a "normal" population.[51, 52. 53]

Most classifications, diagnostic and treatment techniques center on the late stage of this malady with severe pain, steatorrhea and malabsorption. Special medical literature and textbooks refer to these conditions as "pancreatic insufficiency". These symptoms occur when only 10 % of exocrine pancreatic function is left. This is not an "insufficiency." This is pancreatic "failure" when the therapeutic opportunities are very limited.

The authors conclude that the pandemic of digestive disorders are strictly interrelated with pandemics of metabolic acidosis and intestinal dysbiosis. The main organs, which suffer from these conditions, are alkaline digestive glands – the liver and pancreas, and subsequently their secretions: pancreatic juice and bile. Acidification of these fluids changes their digestive capability and triggers the majority of gastrointestinal disorders.

The final stage of chronic pancreatitis does not develop overnight. There are usually 8 - 15 years between the first attack of acute pancreatitis and pancreatic failure after chronic pancreatitis. Similar to disorders of many other organs and systems, the pancreas initial diseased stage does not display any structural changes. However, after this stage, long-standing biochemical, neurohumoral, and inflammation factors lead to structural changes of the pancreas (chronic pancreatitis) and lowering the exocrine pancreatic function while developing many accompanying digestive diseases.

Unfortunately, these diseases deteriorate the exocrine pancreatic function causing many vicious circles. Thanks to human physiology, the pancreas has an enormous 90% functional capacity. However, when this capacity is depleted, the pancreatic failure occurs with steatorrhea, and

malabsorption syndrome, resulting in a total crush of the digestive system and consequently of the whole human organism.

Putting into account that the pancreas is a key digestive organ, the authors propose a practical functional clinical classification of exocrine pancreatic disorders, which involve most of the gastrointestinal disorders and diseases. This functional clinical classification may assist primary care physicians, gastroenterologists and many health professionals in their everyday practice. This clinical classification may help a large number of patients suffering from gastrointestinal disorders to get help in either the early or compensated stages of their condition to avoid pancreatic failure.

Biotherapy Functional Clinical Classification of Exocrine Pancreatic Disorders subdivides all digestive disorders and diseases into three groups.

1. Acidic pancreas and bile

2. Pancreatic deficiency

3. Pancreatic failure

Biotherapy Functional Clinical Classification of Exocrine Pancreatic Disorders takes the common digestive symptoms such as pain, gas, stool, and food sensitivity along with their frequency, quality and changes with a combination of common clinical medical diagnoses and tests.

In everyday medical practice, the crowds of individuals with digestive symptoms consist of patients with the "*acidic pancreas and bile*" stage of exocrine pancreatic disorders. Their tests are usually normal and most of these patients receive palliative symptomatic therapy. The authors consider and try to prove that the acidifying of alkaline digestive glands (pancreas and liver) decreases digestive capacity of pancreatic fluid and bile.

Acidifying also makes these fluids corrosive and "aggressive". This, in turn, causes a large number of pathological refluxes. Improperly digested food is collected and fermented inside. Then, the improperly digested food irritates the walls of the digestive organs causing gas, belching, bloating, abdominal cramps and pain, ulcers, constipation, etc. To eliminate this toxic undigested food, the GI tract has only two openings: the mouth and anus. Nausea, vomiting, and diarrhea are natural detoxification reactions to poor digestion.

Nowadays, a pandemic of interrelated metabolic acidosis, low pancreatic function, and intestinal dysbiosis make a vicious circle and aggravate the clinical digestive symptoms picture.

Restoration of the normal acid – alkaline balance by diet, drinking Karlovy Vary healing mineral water and using some botanicals and food supplements have helped many Europeans with different kinds of digestive problems for a hundreds of years. No doubt, it can be helpful for many Americans, as well.

I. ***Acidic pancreas*** (usually combines with ***acidic bile***)

Symptoms are reversible:

Pain: infrequent abdominal cramps after heavy meals or alcohol intake

Gas and bloating: occurring frequently after heavy, fatty/protein and starchy/ sugary mixed meals

Belching: frequent after heavy, fatty/protein and starchy/ sugary mixed meals

Nausea/Vomiting: rarely

Heartburn: frequent after heavy, fatty/protein and starchy/sugary mixed meals

Stool: tendency to constipate while alternating with constipation/loose stool

Deficiencies of the following nutrients: bicarbonate, minerals, trace elements, vitamins, natural enzymes, probiotics, etc

Food Sensitivity: possible to milk and wheat

Weight: tendency to gain weight and belly fat

Well-being: Most people consider themselves practically healthy and rarely have "sick-days"

The ability to obtain the pancreas histology is limited so an early diagnosis of the pancreatic disorders is often misdiagnosed. Imaging and conventional blood tests usually don't reveal any abnormalities in the functional *acidic pancreas and bile* stage.

Some helpful diagnostic approaches:

- Checking the pH of saliva and urine at a minimum of once per week to verify a tendency toward metabolic acidosis

- Undertaking a *Comprehensive Stool Analysis*

- Undergoing a hydrogen breath test, metabolic panel test and liver panel test

Possible diseases and conditions associated with acidic pancreas and bile stage: functional dyspepsia, biliary dyskinesia, GERD, Sphincter of Oddi Dysfunction type III, IBS, Intestinal Dysbiosis (Candida-yeast overgrowth), metabolic syndrome, etc.

II. ***Pancreatic Deficiency***

Symptoms are steady with a tendency to exacerbate, but can be reversed to the stable remission:

Pain: attacks of abdominal pain and cramps mostly in the epigastria area. Intermittent pain may last from hours to days. May be worsened by eating or drinking alcohol

Gas, bloating: frequent after heavy, fatty/protein and starchy/ sugary mixed meals

Belching: often after heavy, fatty/protein and starchy/ sugary mixed meals

Nausea/Vomiting: can accompany the abdominal pain

Heartburn: often after heavy, fatty/protein and starchy/sugary mixed meals

Stool: tendency to constipate while alternating with constipation/loose stool. Sometimes stool may be pale or clay-colored

Deficiencies of the following nutrients: bicarbonate, minerals, trace elements, vitamins, natural enzymes, probiotics, etc

Food Sensitivity: many food intolerances

Weight: more or less stable with a tendency to gain weight and develop belly fat

Well-being: Fatigue, low energy, depression and insomnia and often complaints of "sick- days"

Possible diseases and conditions associated with pancreatic deficiency: clinical or subclinical episodes of acute pancreatitis, chronic pancreatitis, GERD, gastritis, gastric ulcers, duodenal ulcers, duodenitis, Sphincter of Oddi Dysfunction type II or III, gallbladder disorders (inflammation, stones, sludge, parasites), conditions post gallbladder removal and some surgeries on the upper GI tract, considerable intestinal dysbiosis (Candida-yeast overgrowth, Small Intestine Bacterial Overgrowth), intestinal parasites, IBD (Crohn's Disease, Ulcerative Colitis), Celiac Diseases, Cystic Fibrosis (early stage), Diabetes, alcohol abuse, some acute and/or chronic poisoning etc.

Some diagnostic approaches:

- Checking the pH of saliva and urine at a minimum of once per week to verify a tendency towards metabolic acidosis

- Undertaking a *Comprehensive Stool Analysis*

- Undergoing blood tests such as serum amylase, lipase, trypsinogen, liver and metabolic panels, etc.

- Undergoing hormone tests such as the secretin stimulation test, the cholecystokinin (CCK) stimulation test and the combined secretin-CCK stimulation test

- Undertaking other various tests such as the intraductal and endoscopic secretin stimulation tests, Stool tests such as fecal fat test, fecal elastase, fecal chymotrypsin, etc. Imaging tests such as the abdominal ultrasound, abdominal CT scans, X-ray, magnetic resonance cholangiopancreatography (MRCP) are frequently employed in the initial diagnostic workup of chronic pancreatitis and other pancreatic disorders. When results of standard noninvasive

imaging tests are negative, endoscopic ultrasound (EUS), or endoscopic retrograde cholangiopancreatography ERCP offer improved sensitivity for early disease.

III. ***Pancreatic failure***

Symptoms are steady and considerable with a tendency to develop frequent exacerbations and aggravation of the pancreatic failure condition:

Pain: persistent 80-90% abdominal pain in the middle of the abdomen mostly in the epigastria area with irradiation to the back. Pain is triggered by food or by alcohol intake

Gas, bloating: constant

Belching: often constant

Nausea/Vomiting: nausea/vomiting can accompany the abdominal pain

Heartburn: can occur

Stool: Significant fat malabsorption results in loose, greasy, floating, foul-smelling stools (called steatorrhea) that are difficult to flush. Stool may be pale or clay-colored

Deficiencies of the following nutrients: usually proteins, fats, fat soluble vitamins (A, D, E, K), vitamin B-12, foliate, bicarbonate, minerals, trace elements, vitamins, natural enzymes, digestive enzymes, probiotics, etc

Food Sensitivity: fat and glucose

Weight: unintentional weight loss and malnutrition

Well-being: exhaustion, significant depression and disablement

Possible diseases and conditions associated with pancreatic failure: final stage of chronic pancreatitis, Cystic Fibrosis, liver cirrhosis, cancer, etc.

Today, conventional medicine, doctors and other health professionals, haven't established therapeutic methods for improving the exocrine pancreatic function and property of bile. Therefore, the primary focus of this book is the healing actions related to ***acidic pancreas and bile*** and ***pancreatic deficiency***, the reversible or partially reversible conditions. However, some recommendations and natural non-drug approaches may be useful for improving the quality of life of individuals with ***pancreatic failure***, as well.

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DISEASES AND DISORDERS WITH DECREASING OF EXOCRINE PANCREATIC FUNCTION

Chapter 8-Pancreas and the Sphincter of Oddi Dysfunction (SOD)

For individuals lacking a medical background

Imagine there are two rivers…

One river is large, clean and clear and flows freely to the sea. This represents the pancreatic duct which moves the pancreatic juices and digestive enzymes into the duodenum. Before flowing into the sea (the duodenum), the first large, big, and clear river spills into a lagoon (the Ampulla of Vater). At the end of the entrance of the lagoon there is a gate (the Sphincter of Oddi), which regulates the water coming into the sea (the duodenum).

The second river is smaller, with yellow, dirty, and greasy water, full of stones and debris. This second river is the bile duct, which moves bile from the liver and gallbladder and merges with the first river near the gate of the lagoon. This gate is operated by an intelligent natural regulating system, which allows both rivers to mix together and flow smoothly into the sea. This natural regulating system is complex of digestive hormones, which are produced in the duodenum.

If there is too much debris in the lagoon, or the natural regulating system crashes and the gate is locked, it causes back up, flooding and many other problems. Rotting debris in the first river causes pancreatitis. Back up of the second river causes inflammation and a shutdown of the liver and/or the gallbladder.

This area is the site where many liver, gallbladder and pancreatic problems occur. Many scientists believe that the Sphincter of Oddi Dysfunction (SOD) is the cause of pancreatic diseases and that restoring proper function of this valve is the correct way to heal congestion and inflammation of the pancreatic gland.

Digestive System Structure

Let's start from the liver. The liver is our body's chemical factory and performs many vital tasks. The most important function of the liver is to manufacture and release bile. The cells of the liver secrete bile into a network of ducts. Like a river, these ducts gradually join to form one stream in the main bile duct, which exits (along with the pancreatic duct) into the duodenum. The Sphincter of Oddi is the muscle valve surrounding the common bile duct and merging with the pancreatic duct. The Sphincter of Oddi opens these ducts into the duodenum. The nervous system regulates this valve through special messengers – the digestive hormones.

If there is no food in the intestine, a valve – the Sphincter of Oddi remains closed, retaining the bile in the bladder and pancreatic juice in the pancreas. Spasm or blockage of this valve may

cause bile and pancreatic juice to back up. Remember, a tiny amount of bile in the pancreatic duct can cause serious trouble. Bile activates digestive enzymes inside the pancreas, and they start to digest their own pancreatic cells, causing pain, congestion, inflammation, even the death of pancreatic tissue.

Tumors, large gallbladder stones and post-inflammatory scars that block the Sphincter of Oddi certainly need surgery. There are not too many cases of individuals needing these surgeries, but millions of Americans suffer from occasional transient spasms of this sphincter with pain, nausea and bloating. In most situations, their tests are normal and these individuals are labeled with acid reflux, IBS, stomach flu, food poisoning or other diseases. Many of these patients have type III Sphincter of Oddi Dysfunction (SOD). Lack of proper treatment of this condition can later cause serious complications like pancreatitis and gallbladder inflammation.

Sphincter of Oddi Dysfunction affects:

- Mostly adults after age forty

- More females than males

- Overweight individuals

- Populations post abdominal surgeries: for example, statistics shows that almost 20% of people after gallbladder removal have the Sphincter of Oddi Dysfunction[4]

Why does this muscle sphincter become spasmodic? It depends on many reasons if we put into account the very complicated regulation of this sphincter by the nervous system and by special blood messengers – the digestive hormones.

Factors That Make the Sphincter of Oddi Spasm:

- Stress, depression and anxiety

- Poor eating habits such as eating too quickly, irregular diet, fasting, wrong combinations of food such as mixing fatty foods with starches and sugars

- Drugs, some medications, alcohol and nicotine

- Harsh, intensive, and repetitive "liver flushing"

- Hormonal imbalances such as lower thyroid function or menopause

- “Aggressive” acidic bile with sand, sludge, gallbladder stones

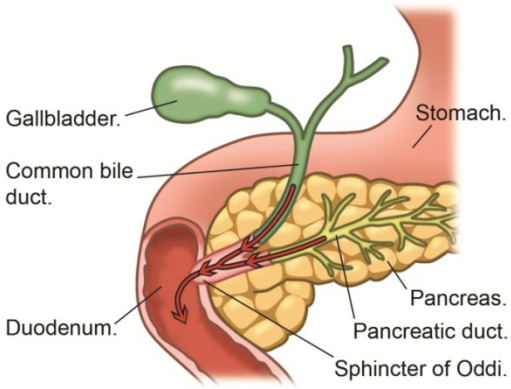
- Upper abdominal surgeries, and more

Usually we can see a combination of these factors over a long period of time in overweight, sedentary and stressed individuals. The Standard American Diet, which is full of processed and acidic food (meat, sugars, alcohol, animal fats, white flower, etc.), causes acidity in the whole body. It leads to an acidic condition in the bile and pancreatic juice.

The very important components of bile are bile acids and bile salts. When the blood keeps minerals and bicarbonates for neutralizing the acid radicals in the blood, the bile cannot receive

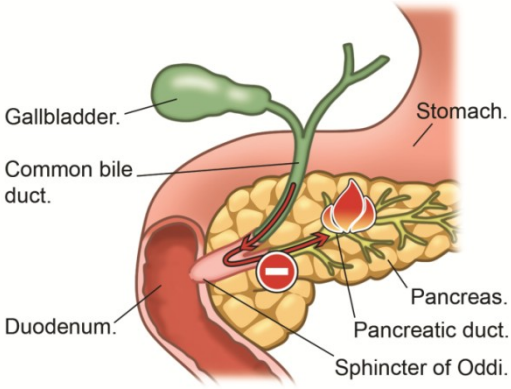
alkaline substances. The bile becomes acidic and the amount of bile acids in the bile increases, as well. Bile acids are very aggressive substances; they irritate the wall of the Sphincter of Oddi, causing muscle contraction – the spasm. This spasm creates the back up of bile and pancreatic juice which leads to pain, cramps, nausea, vomiting, abdominal bloating and discomfort after eating, alternation of stool (constipation, diarrhea) - all symptoms of the Sphincter of Oddi Dysfunction.

Normal moving of bile and pancreatic juice



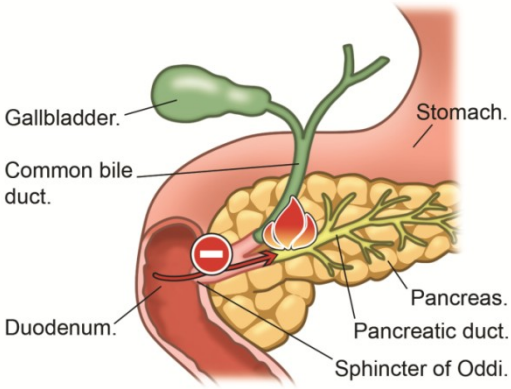
In healthy condition, mix of the bile and pancreatic juice go down to the first part of the small intestine that is called duodenum. Alkaline environment in the duodenum is important factor of the good digestion and proper movement of the digested food down to the lower parts of the small intestine. Acidifying of bile makes this fluid very “aggressive”. It irritates valves, ducts, duodenum wall causing jerk moving, and back flow of bile – bile reflux.

Bile reflux into the pancreas due to blockage of sphincter of Oddi



Blockage of sphincter of Oddi can increase the pressure inside the pancreatic duct. This can cause mix of the bile and pancreatic juice reflux back into the pancreas. Even small amount of the bile can activate pancreatic enzymes inside the pancreas leading to irritation, inflammation and finally damage and death of the pancreatic tissue.

Bile reflux into the pancreas due to opening of sphincter of Oddi



If sphincter does not closed tightly, content of duodenum with bile and active pancreatic enzymes can reach and injure pancreas through opening of sphincter of Oddi.

It can happen due to mechanical reasons such as inflammation, surgery, slipping of the large gallbladder stones, high pressure inside the duodenum due to collecting of gas and fluids, etc., and/or lack of proper nervous and hormonal regulation of sphincter contraction due to gallbladder removing, medication, alcohol, drugs, poor diet, stress, etc.

If the spasm of the Sphincter of Oddi is prevalent in the common bile duct, pain is felt mainly in the middle or right part of the upper abdomen. If the spasm involves the pancreatic duct, pain is located in the upper abdomen on the left or right side and radiates directly through the abdomen to the back. This attack of pain brings individuals to the hospital, but in cases of the most prevalent Sphincter of Oddi Dysfunction type III – the tests are normal and the patient is discharged with vague advices not to consume alcohol and spicy and fatty foods.

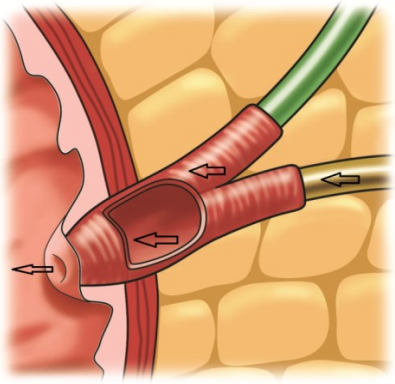
Even the initial attack of pain in the upper stomach area can be a signal to the beginning of Sphincter of Oddi Dysfunction that can start the deadly chain:

Sphincter of Oddi Dysfunction =>pancreatitis => pancreatic cancer.

The Sphincter of Oddi is a central gate to many liver, gallbladder and pancreas problems. Many scientists believe that the Sphincter of Oddi Dysfunction (SOD) is a culprit of the pancreas diseases. However, if the valve is functioning properly, then it helps in healing congestion and inflammation of the pancreatic gland

For individuals with medical backgrounds

The Sphincter of Oddi, named after Ruggero Oddi, an Italian anatomist who described this structure in 1887, is the valve muscle that regulates the flow of bile and pancreatic juice into the duodenum (beginning of the small intestine). This muscle valve surrounds the common bile duct and pancreatic duct and their opening into the duodenum. (See the normal bile and pancreatic juice flow in the picture).



The Sphincter of Oddi has three main functions:

- To regulate flow of the bile and pancreatic juice into the duodenum

- To prevent backflow of bile and pancreatic juice (reflux) from the duodenum to the bile and pancreatic ducts

- To fill up the gallbladder with liver bile[78]

a. The Pancreas and the Sphincter of Oddi

The cells of the pancreas secrete enzymes into a network of small ducts that ultimately drain into the pancreatic duct. The pancreatic duct merges with the common bile duct at the Ampulla of Vater. The pancreatic juice mixes with the bile and is forced through a muscular valve called the Sphincter of Oddi. The Sphincter of Oddi is a sphincter, which is strategically placed at the junction of the bile duct and pancreatic duct with the duodenum.

The sphincter of Oddi is comprised of smooth muscle fibers that surround the end of the pancreatic duct and the end of the common bile duct. A properly functioning Sphincter of Oddi contracts and relaxes accordingly to let out the appropriate amounts of bile and pancreatic juice with digestive enzymes to allow for the digestion of food. Sphincter of Oddi Dysfunction may be related to either the pancreatic or the biliary segments of the sphincter, or both.

A properly functioning Sphincter of Oddi is critical to the health of the entire gastro-intestinal system – and necessary for a healthy body.

Many scientists believe that Sphincter of Oddi Dysfunction (SOD) causes the beginning of many pancreatic diseases. So, healing an injured and malfunctioned Sphincter of Oddi can reduce congestion and inflammation of the pancreatic gland

b. The Gallbladder and the Sphincter of Oddi

After the partially digested food (chyme) goes into the duodenum, the gallbladder contracts and the Sphincter of Oddi relaxes leading to delivery of bile to the duodenum. At the end of the meal, the gallbladder relaxes and the Sphincter of Oddi contracts leading to the diversion of the hepatic bile into the gallbladder once again for storage until the next meal.[78] The gallbladder and the Sphincter of Oddi are very tightly connected and regulated because the similar nerves and digestive hormones such as cholecystokinin and secretin regulate their contraction and relaxation.

Both increased and decreased Sphincter of Oddi pressures have been reported during biliary pancreatitis. Elevated pressures are thought to predispose patients to gallstone impaction or elevated pancreatic duct pressure. Decreased Sphincter of Oddi pressure can lead to free reflux of duodenal contents into the pancreatic duct.

c. Sphincter of Oddi Dysfunction (SOD)

According to information from the 1993 *"U.S. householder survey of functional diseases"* by Drossman DA *et al*. the prevalence of Sphincter of Oddi Dysfunction in the general population is 1.5% [203]. This equates to 4.5 million people in the US suffering from SOD.

There are two overall factors, which influence the proper functioning of the Sphincter of Oddi:

1. Anatomical (structural) integrity
2. Functional ability

For smooth performance, the anatomical integrity of the Sphincter of Oddi must remain intact. For example, a physical blockage of this valve may stop the smooth flow of pancreatic fluid and bile. Gallstones or tumors can cause the blockage of the Sphincter of Oddi. The mix of bile and pancreatic juice becomes backed up and increases pancreatic duct pressure. The bile initiates enzymes to start digesting the pancreatic cells, which causes severe inflammation, pain and finally the death of pancreatic tissue.

If the mixture backs up into the bile duct, the result may be hepatitis, jaundice or bile ducts' inflammation. The anatomical narrowing or closing of the Sphincter of Oddi is relatively rare, but may be caused by large gallbladder stones, severe inflammation, scars or tumors. In these cases, surgical care is necessary. On the other hand, surgical injury of the Sphincter of Oddi (sphincterotomy) can cause backflow of the duodenum's content into the pancreatic duct, as well.

Multiple things can cause structural blockages of the Sphincter of Oddi including: pancreatitis (inflammation of the pancreas), infection, parasites, fat deposits due to being overweight or obesity, trauma, surgery and cancer. These structural damages of the Sphincter of Oddi usually require years for developing.

More frequently, individuals have problems with the functional ability of the Sphincter of Oddi. A frequent functional problem involves spasms of the sphincter opening, or dyskinesia (In Latin "*dys*" means abnormal, "*kinesia*" means movement).

Conventional medicine offers little in the way of diagnosis, treatment, and prevention at the beginning of SOD. Lack of diagnosis and treatment can later cause serious complications such as pancreatitis and gallbladder inflammation.

When the bile and pancreatic juices are not let through the Sphincter of Oddi into the duodenum, they can become backed up which can lead to abdominal pain and other symptoms such as nausea and vomiting. This Sphincter of Oddi dysfunction has been described in patients who present recurrent biliary or pancreatic pain and no evidence of a structural cause for the pain and normal tests.

Based on clinical evidence, scientific researches and our personal medical experience, we speculate that the initial stage of the Sphincter of Oddi Dysfunction (referred to as type III Sphincter of Oddi Dysfunction) starts from two important things: improper nervous and/or digestive hormone regulation of the sphincter and the abnormal quality and quantity of pancreatic juice and bile.

d. How Does the Sphincter of Oddi Dysfunction Occur?

The brain sends signals to the Sphincter of Oddi to regulate the release of the digestive juices according to our food intake. For example, more bile is released for consuming fatty meals. Connections between nervous system conditions and proper digestion are well-known facts. There are many autonomic neural connections between the Sphincter of Oddi, gallbladder, and duodenum. In addition to digestive hormones, these nerves are important in the control of the Sphincter of Oddi motility and function.

Various lifestyle issues such as depression, stress, anxiety, some medications, alcohol, recreational drugs (especially opiates), irregular diets, fasting, wrong combinations of food, "eating on the go", hormonal changes (lower thyroid, pregnancy, menopause), sedentary life styles, lack of exercise and metabolic acidosis can cause spasms of the Sphincter of Oddi.

These elements influence the proper release and function of the digestive hormones secretin and cholecystokinin, which are the natural regulators of the Sphincter of Oddi.

On the other hand, to function properly, pancreatic enzymes require the pH of the duodenum to be alkaline. Because the food coming from the stomach has recently been acidified, the body must provide enough excess alkalinity in the duodenum for the enzymes to work. Sufficient amounts of water, minerals, trace elements, and bicarbonates have a crucial impact on the alkalinity of bile and pancreatic juice, and therefore quality and the proper amount of the pancreatic digestive enzymes.

Certain lifestyle factors such as consuming acid-forming food can cause metabolic acidosis, or, in other words, an excess of overall acidity in the body. Smoking, alcohol, drugs, and Candida-yeast overgrowth can also increase body acidity. If the body is acidic, the pancreatic juice and bile become acidic, as well. Acidic bile is very "aggressive." It irritates and corrodes the surrounding tissues leading to spasms, pain, ulcers and pancreatitis. Acidic, "aggressive" and toxic bile can irritate the Sphincter of Oddi causing dyskinesia and spasms and increasing pressure into the pancreatic duct.

Regularly drinking alcohol with food can harm the Sphincter of Oddi function.

Tierney S *et al. (*1998) [202] demonstrate that, "ethanol infusion inhibits both the Sphincter of Oddi amplitude and motility index and that this effect persists for at least 20 minutes following ethanol infusion." Ethanol may also contribute to gallstone formation by altering biliary sphincter motility.

In 2001, doctors Frulloni, L. and Cavallini, G. from the Department of Surgical and Gastroenterological Sciences at the University of Verona in Italy proposed that almost 20% of pain following surgery to remove a gallbladder, might be connected to SOD. Italian doctors also believed that Sphincter of Oddi Dysfunction is a common cause of acute recurrent pancreatitis, and may account for up to one-third of the unexplained cases of this dangerous disease.[87]

Millions of Americans suffer from occasional transient spasms of this sphincter with pain, nausea and bloating. Many of these sufferers have type III Sphincter of Oddi dysfunction. Sphincter of Oddi type III has been described in people that present recurrent biliary or pancreatic type pain with no evidence of a structural cause for the pain. Their medical tests usually are normal.

Understanding the cause of the problem can help in healing. In the past several years, evidence has emerged of an association between SOD, intestinal dysmotility and visceral hyperalgesia. [77]

The most common and prominent symptom of SOD is upper abdominal pain. This is often experienced as a sharp pain in the middle of the abdomen right below the rib cage. Pain can be severe in nature, sending individuals to the hospital and requiring pain medication. But in many cases, pain may be mild and usually does not need painkillers. Symptoms of SOD are divided as biliary pain and pancreatic pain.

e. Symptoms of Sphincter of Oddi Dysfunction

Symptoms of Sphincter of Oddi Dysfunction Biliary Pain Include:

- Biliary pain felt in the middle or right part of the upper abdomen
- Pain radiating on the back at the lower tip of the scapula or right shoulder
- Pain can be accompanied by bloating, nausea and vomiting
- Pain precipitated by fatty food or alcohol
- Pain may vary in intensity and can last anywhere from 15 minutes to 4-5 hours

Symptoms of Sphincter of Oddi Dysfunction Pancreatic Pain Include:

- Pain that is located in the upper abdomen on the left or right side
- Pain that radiates directly through the abdomen to the back
- Pain can often be accompanied by bloating, nausea and vomiting
- Pain precipitated by the wrong combination of protein/fat/starch/sugar foods or consumption of alcohol

Some patients describe debilitating pain that brings them to the Emergency Department several times a year and keeps them from living a normal life.

f. Who is affected by SOD?

Sphincter of Oddi Dysfunction can occur in anyone, but it is most often seen:

♦ In women between the ages of 30 and 50

♦ In small children where pain manifests in the navel area and causes poor appetite, nausea and vomiting after eating fatty and sugary foods

♦ In large children where pain can be acute in the upper right abdominal area during running, dancing and playing; some children complain of bitter taste in the mouth

♦ In smokers after eating a fatty meal with alcohol

♦ In individuals after "harsh" liver cleansing and fasting

♦ In patients with removed gallbladders or other upper abdominal surgeries

The authors of this book focus mainly on Type III Sphincter of Oddi Dysfunction patients. This condition is characterized by biliary or pancreatic pain and no other documented abnormalities in the non-invasive tests. Type III Sphincter of Oddi Dysfunction is a functional reversible condition that is commonly misdiagnosed or ignored. Proper actions may postpone many serious problems such as gallbladder stones and inflammation or billiary pancreatitis.

Some specialists conclude that the patient can wait until confirming a diagnosis by measuring the pressure inside the Sphincter of Oddi using manometry during an ERCP (Endoscopic Retrograde Cholangio-Pancreatography).

Cheng *et al.* (2006) in the article, *Risk Factors for Post-ERCP Pancreatitis: A Prospective Multicenter Study* published *in American Journal of Gastroenterology* focus on SOD and ERCP. These authors found that all ERCP's may result in complications with the most common (6-15%) being inflammation of the pancreas (pancreatitis).[174]

Interesting facts at a glance:

The Sphincter of Oddi is a smooth muscular valve that surrounds the common bile duct and the pancreatic duct

The Sphincter of Oddi is strategically placed at the junction of the bile duct and pancreatic duct with the duodenum

The Sphincter of Oddi has three main functions: regulating the flow of bile and pancreatic juice into the duodenum, preventing reflux from the duodenum to the bile and pancreatic ducts and filling up the gallbladder with liver bile

The gallbladder, pancreas and the Sphincter of Oddi can act in concert with one another because similar nerves and digestive hormones, such as cholecystokinin and secretin, regulate the functions of these organs

A frequent functional problem involves spasms of the sphincter opening, or dyskinesia. Both problems can cause the Sphincter of Oddi Dysfunction (SOD)

Prevalence of the Sphincter of Oddi Dysfunction (SOD) in the general US population is 1.5%; this equates to 4.5 million sufferers from SOD

Depression, stress, anxiety, some prescription medications, alcohol, recreational drugs (especially opiates), irregular diet, fasting, the wrong combinations of food, "eating on the go", hormonal changes (lower thyroid, pregnancy, menopause), sedentary lifestyles, lack of exercise and metabolic acidosis may trigger SOD

Acidic diet, alcohol and Candida-yeast overgrowth may cause the initial stage of SOD, or type III Sphincter of Oddi Dysfunction

Acidic and "aggressive" toxic bile can also irritate the Sphincter of Oddi causing dyskinesia and spasms, thereby increasing pressure in the pancreatic duct

SOD may contribute to the risk of acute pancreatitis by causing abnormal biliary or pancreatic juice flow. There is also evidence-linking SOD with chronic pancreatitis

After the gallbladder is removed, almost 20% of people have some degree of Sphincter of Oddi Dysfunction

The most common symptom of SOD is upper abdominal pain. This is often experienced as a sharp pain in the middle of the abdomen. Bloating, nausea, and vomiting can accompany pain. Pain is precipitated by fatty food or alcohol. The pain may vary in intensity and can last anywhere from 15 minutes to 4-5 hour

Type III Sphincter of Oddi Dysfunction is a functional reversible condition that is commonly misdiagnosed or ignored

Proper actions may postpone many serious conditions such as gallbladder stones, inflammation or billiary pancreatitis

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Chapter 9-Pancreatitis. Acute Pancreatitis

For individuals with a medical background

Pancreatitis is a mysterious condition due to the medical community lacking a full picture of what the disease consists of. Each specialist diagnoses the problem based upon his or her professional and clinical experience.

To describe such a serious problem as pancreatitis, let's begin with various quotes from published documents of experts in this medical field..

Michael L. Steer, M.D., Irving Waxman, M.D., and Steven Freedman, M.D from the Departments of Surgery and Medicine, and the Pancreatico-Biliary Diseases Center, Beth Israel Hospital and Harvard Medical School, Boston in "*Chronic Pancreatitis" (N Engl J Med* 1995; 332:1482-1490) quote:

"In 1788 Cawley reported on a "free living young man" who had died of emaciation and diabetes and whose postmortem examination revealed multiple pancreatic calculi. In the two centuries since that early description of chronic pancreatitis, literally thousands of reports dealing with this disease have been published, yet chronic pancreatitis remains an enigmatic process of uncertain pathogenesis, unpredictable clinical course, and unclear treatment".[89]

Or, from the book *Chronic Pancreatitis* by M.W. Buchler, H. Friess, W.Uhl, P. Malfertheiner. 2002. p.8. Blackwell Publishing:

"In the absence of minimal evidence for etiology, the identification of a mechanistic explanation of the disease process has been similarly frustrating.

As a result of the absence of a defined etiology and lack of mechanism of disease, clinical attention to chronic pancreatitis has for the most part focused on establishing of a diagnosis and thereafter management of the sequelae, including pain, ductal obstruction, and the exocrine and endocrine deficits based upon acinar and islet cell destruction.

The natural history of chronic pancreatitis with development of endocrine and exocrine insufficiency, leading to diabetes and steatorrhea, provide further supportive clinical evidence.

Since no definitive treatment exists, the evolution of therapy has perforce been directed at dealing with the symptomatic manifestation of the disease".[17]

Yamada T, Alpers DH, Laine L, Owyang C, Powell DW. *Textbook of Gastroenterogy*. 3rd ed. 1999, p. 2107, by Lippincott publishers quote:

"Diseases of the pancreas are often more difficult to manage medically or surgically than those of other abdominal viscera."[81]

a. History of Pancreatitis:

Pre-1896: Pancreatitis classified as an infection

1896: Pancreatitis is classified as pancreas auto digestion by its own digestive enzymes

1901: Pancreatitis is determined to be caused by gallstones and ranked between biliary diseases and pancreatic pathology

1946: A connection between alcohol abuse and chronic pancreatitis is discovered

1959: Dietary factors (low protein, fat-deficient diet) are determined to potentially cause chronic pancreatitis

1996: Hereditary Pancreatitis is discovered to be caused by mutations in the cationic trypsinogen gene (PRSS1) and premature trypsinogen activation

b. Frequency and Epidemiology of Pancreatitis

United States

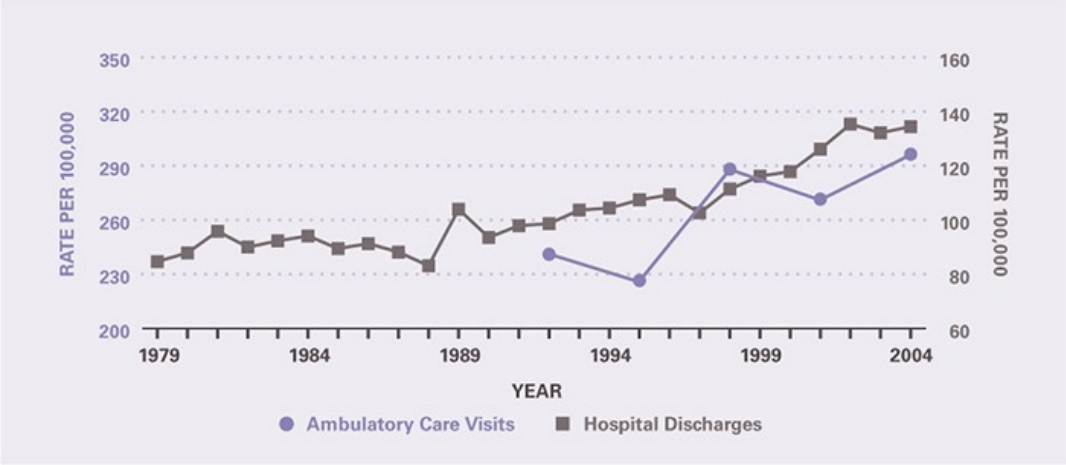
Based on estimates from hospital discharge data in the United States, approximately 87,000 new cases of pancreatitis occur annually.

In 2004, according to the US Department of Health and Human Services, there were 881,000 ambulatory care visits due to pancreatitis. The rates of hospital pancreatitis visits increased moderately with age.[109]

Between 1979-2004, age-adjusted rates were 25 percent higher among blacks than whites, and 52 percent higher among females than males. Pancreatitis was the seventh most commonly noted hospitalized digestive disease diagnosis, just after peptic ulcer disease.

Hospitalization rates increased with age and were 88 percent higher among blacks, and were 11 percent higher among males. Rates of both ambulatory care visits and hospitalizations with pancreatitis increased from the 1979 to 2004 (Figure 1). In particular, the rate of hospital discharges with a pancreatitis diagnosis increased 62 percent between 1988 and 2004.

Figure 1. Pancreatitis: Age-Adjusted Rates of Ambulatory Care Visits and Hospital Discharges with All–Listed Diagnoses in the United States, 1979–2004[109]



Everhart JE, editor. The burden of digestive diseases in the United States. US Department of Health and Human Services, Public Health Service, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases. Washington, DC: US Government Printing Office, 2008; NIH Publication No. 09-6443.[109]

Pancreatitis ranked eighth among all digestive diseases prior to age 75, with about 43,000 years potential life lost to age or 12.3 years per death. Death rates increased with age and were higher among blacks than whites and men than women. In 2004, pancreatitis was the eleventh most common underlying cause of death from digestive diseases and the fifth most common nonmalignant cause, just after peptic ulcer disease. More than half of deaths occurred among individuals are age 65 years and older. The study also shows that pediatric pancreatitis increased 53% in children from 1995 to 2006.

Information about chronic pancreatitis is particularly difficult to assess because of the confusion of definitions between acute pancreatitis, acute recurrent pancreatitis, and chronic pancreatitis. Furthermore, only recently have there been uniform guidelines for the diagnosis of chronic pancreatitis.[17]

More than 25 million people in the United States suffer from liver, bile duct, or gallbladder diseases, according to the American Liver Foundation. Since the function and diseases of the liver, gallbladder, bile ducts and pancreas are all closely associated, this will give an idea about the prevalence of pancreatic disorders too.

The only available information regarding the occurrence of chronic pancreatitis comes in reports from specialized medical centers treating these disorders. Such reports suffer from a bias that patients with these difficult diseases could be selectively referred to treatment centers specializing in management of pancreatitis.

Altogether, these statistics illustrate that reported frequencies of the new cases of chronic pancreatitis in different kinds of populations in the world are estimated at 7-10/100,000 per year. Nearly all of these patients confirmed this diagnosis by CAD scan. This data makes the conclusion that chronic pancreatitis is an uncommon disease.[17]

However, these statistics include only severe cases with pain and maldigestion that require hospital care. By the authors' opinions, this is only the tip of the iceberg, because hundreds of thousands of individuals with mild forms of chronic pancreatitis are either treated by PCP, or do not seek medical attention at all, and thus, are not included in these statistics. These individuals, especially older adults, suffer from a different kind of maladies due to progressive insistent exocrine pancreatic deficiency and neither doctors nor those individuals are aware of the problem.

International

Comparing the hospital admissions data from several cities around the globe, the overall frequency is similar to the US statistics. When data from several centers are compared over time, the incidence of chronic pancreatitis appears to be increasing.[15]

Between 1989-1990 and 1999-2000, English hospital admission rates for acute pancreatitis increased by 43%, while those for chronic pancreatitis rose by 100%.[18]

Scandinavian doctors Rothenbacher D. *et al*. (2005) investigated the prevalence and main determinants of exocrine pancreatic insufficiency in a large population-based sample of older adults by measuring pancreatic elastase-1 in stool. From the 914 subjects, 11.5% of the subjects showed signs of exocrine pancreatic insufficiency and 5.1% of the subjects showed signs of a severe exocrine pancreatic insufficiency.[19]

Pancreatitis or pancreatic fibrosis appears to be frequent in Western societies and might affect more than 10% of the subjects in population-based studies[51]

Acute Pancreatitis

Acute pancreatitis occurs when the pancreas quickly becomes severely inflamed. In our opinion, the major causes of acute pancreatitis are:

>Heavy alcohol ingestion/binge drinking

>Gallstones or gallbladder disease

>Trauma, abdominal surgery and endoscopic manipulation

>Drugs

> Severe dehydration

>Fatty pancreas and high blood fats

>Heredity factors

>Cystic fibrosis

>Infections such as mumps, hepatitis A or B, salmonella, etc

Binge alcohol drinking is a common cause of acute pancreatitis but not all alcoholics have a history of pancreatitis.

Gallbladder disease, especially where a gallstone becomes lodged in the main bile duct next to the pancreas, can cause acute pancreatitis. Acute pancreatitis may develop after gallbladder removal or even without the big stones in the bile ducts. For most cases of acute pancreatitis there are predisposed reasons and factors that causes a "willingness" for aggression of pancreatic digestive enzymes to self digest their own pancreas. This can only occur when the pancreatic inhibitor system that suppresses proteases (trypsin) to digest their own cells has failed. Premature activation of pancreatic enzymes within the pancreas leads to organ injury and pancreatitis.

In 2007, nearly 220,000 patients with acute pancreatitis were expected to be admitted to non-federally funded hospitals in US. In 1998, 183,000 patients with acute pancreatitis were admitted. This trend in rising incidence has been recognized over the past several decades.[11]

The main symptoms of acute pancreatitis are severe pain in the upper abdomen, vomiting, and fever. Acute abdominal pain may be localized at the back and upper left abdomen and is relieved by leaning forward. In mild cases, the pain may last 2 to 3 days; the short-term prognosis in such cases is good. In severe cases, however, the pain may persist for several weeks and the risk of death rises to about 30 percent. [2] Acute pancreatitis is life threatening and requires hospitalization and intensive care. Mortality of acute pancreatitis is usually 10-15%.

The scope of this book it is not intended to focus on acute conditions, but on actions to help individuals avoid this serious condition.

Interesting facts at a glance:

Pancreatitis is a mysterious condition

Based on estimates from hospital discharge data in the United States, approximately 87,000 new cases of pancreatitis occur annually

In 2004, according to the US Department of Health and Human Services, there were 881,000 ambulatory care visits due to pancreatitis

Rates of both ambulatory care visits and hospitalizations with pancreatitis increased from the 1979 to 2004

In 2004, pancreatitis was the eleventh most common underlying cause of death from digestive diseases and the fifth most common nonmalignant cause, just after peptic ulcer disease

Information about chronic pancreatitis is particularly difficult to assess because of the confusion of definitions between acute pancreatitis, acute recurrent pancreatitis and chronic pancreatitis

Statistics include only severe cases with pain and maldigestion that require hospital care

This is only the tip of the iceberg, because hundreds of thousands of individuals with mild forms of chronic pancreatitis are either treated by PCP or do not seek medical attention at all

Pancreatitis or pancreatic fibrosis appears to be frequent in Western societies. By population-based studies, it might affect more than 10% of the population

In 2007, nearly 220,000 patients with acute pancreatitis were expected to be admitted to non-federally funded hospitals in US

Acute pancreatitis is life threatening and requires hospitalization and intensive care. Mortality of acute pancreatitis is usually 10-15%

Preventive measures to help individuals avoid acute pancreatitis are extremely important

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Chapter 10-Chronic Pancreatitis

For individuals with a medical background

At this time, there is no consensus between specialists about exactly what pancreatitis, recurrence of acute pancreatitis, chronic pancreatitis, exacerbation of chronic pancreatitis, flare of chronic pancreatitis, pancreatic insufficiency and pancreatic deficiency are. Therefore, since there is no agreement on what the diseases are, there is no consensus on treating them. This is still a matter of debate between scientists, physicians, gastroenterologists, and surgeons.

"Despite considerable attention to the identification of the basis of chronic pancreatitis, approximately 30% of patients diagnosed with the disease still are regarded as idiopathic with no

known evidence of any associated disease or inciting event. In the absence of minimal evidence for etiology, the identification of a mechanistic explanation of the disease process has been similarly frustrating."

M.W. Buchler *et al*." *Chronic Pancreatitis*". 2002.[17]

Pancreatitis can manifest as a one-time episode, recurring attacks, or chronic pain. It is caused by numerous factors ranging from alcohol consumption to gallstones, to subtle obstructive causes and occult autoimmune disorders. As a result, determining the etiology and effectively treating the causes and consequences of pancreatitis can be challenging.

Kinney, T.P. and Freeman M.L. in the article "*Approach to acute, recurrent, and chronic pancreatitis*" in 2008 underlined:

"Like most medical disorders, pancreatitis can manifest in a variety of ways, from severe, fulminatory, and a life-threatening disease to an ongoing or "smoldering" disease with minimal laboratory abnormalities. Some patients experience a single episode, while others can have recurrent attacks. Still others with minimal-change chronic pancreatitis may present only with intractable pain. Thus, in some patients, pancreatitis can be difficult to diagnose and treat".[13]

David C Whitcomb, MD the acknowledged authority in pancreatic diseases stated that "Chronic pancreatitis remains a challenging and frustrating clinical problem" and "Chronic pancreatitis comprises a spectrum of disorders that culminate in the destruction of the pancreas".

Unfortunately, imaging studies and functional tests usually cannot detect chronic pancreatitis in its earliest, potentially reversible stages, and pancreatic biopsies are rarely performed for fear of triggering acute pancreatitis or other complications.

Chronic pancreatitis may be caused by the following factors:

1. Recurrent injury: can be caused by activation of the pancreatic digestive enzyme (trypsin) inside the pancreatic (acinar) cells or inside pancreatic ducts. The inactive form of trypsin called trypsinogen starts premature activation and becomes the active form - trypsin that self digest its own pancreas, thus leading to inflammation

2. Persistent inflammation: can be caused by the process of activating non-active trypsinogen to become active trypsin

3. Significant anti-inflammatory response (driving fibrosis) [12] can lead to the destruction of pancreatic cells and to the replacement of functional pancreatic tissue by scaring tissue, thus changing of structure of the gland and loss of it function

Premature trypsinogen activation and persistent trypsin activity inside the pancreas is the key factor of pancreatic injury. Therefore, control of trypsin is the key to controlling digestive enzyme activation and pancreatic injury

a. History of Chronic Pancreatitis

Chronic pancreatitis was first described more than 200 years ago.

1889: R. Fitz defined the signs and symptoms of pancreatitis.

1901: E. Opie advanced the hypothesis whereby acute pancreatitis was the aftermath of infected bile flowing into the pancreatic duct from the common bile duct, when the gallstones caused obstruction.

1919: E. Archibald demonstrated that spasms of the Sphincter of Oddi, increased biliary pressure and culminated in the development of acute pancreatitis.

In recent years, there have been many discoveries in genetic mechanisms for several inherited causes of chronic pancreatitis made by **David C Whitcomb, MD** and other researchers.

Chronic pancreatitis has been studied by thousands of scientists, MDs, gastroenterologists, surgeons biochemists and genetic researchers for many decades, but as stated by M.W. Buchler *et al*. (2002), "unfortunately the cause of acute and especially chronic pancreatitis remains shrouded in dogma and conjecture".[17]

Many pancreatic studies focus on the advanced stage of chronic pancreatitis with severe pain and maldigestion when the structure and function of the pancreas is too compromised. At this stage, even brilliant medical minds, knowledge, and virtuosic diagnostic and surgery techniques are too late to treat this severe irreversible condition.

Therefore, the authors of this book repetitively consider that it is necessary for therapeutic results to focus on early stages of the pancreatic injury.

After the first sentinel event in individuals, which are at risk of unregulated trypsin activation inside the pancreas, or after the first episode of acute pancreatitis occurs, all clinical attention has to focus on delaying the development of pancreatic failure, severe maldigestion, pain, and metabolic disorders.

b. Chronic Pancreatitis Definition

Chronic pancreatitis (CP) is the progressing gradual inflammation of the pancreas, which causes permanent tissue damages and gradual scarring replacement of pancreatic tissue.

According to Professor David C Whitcomb, MD, "Chronic pancreatitis remains a challenging and frustrating clinical problem."[12] The pancreatic tissue is constantly lost, and in turn, leads to the final stage of the disease with the decreasing of digestive pancreatic enzyme production (malabsorption) and insulin deficiency diabetes. Pain and diarrhea persist mostly in the advanced

stage of CP when therapeutic actions are becoming restricted. The resulting symptoms of abdominal pain and maldigestion are frequently complicated by malnutrition, psychosocial decline, work-loss, narcotic/alcohol addiction and large health care expenditures.

c. Who is at Risk for Chronic Pancreatitis?

Inflammation and the destruction and loss of pancreatic function are influenced by: diets, lifestyles, environmental chemicals, infection, intoxication, medications, parasites, surgery, heredity and gene mutations. The authors believe that diets, lifestyles and environmental chemicals have the most direct impact for developing acute and chronic pancreatitis. Historically, we are not the first to entertain this idea.

1788: Cawley became the first to suggest the link between lifestyles and pancreatic disease[20]

1946: M. Comfort described in detail the connection between alcohol abuse and chronic pancreatitis

1959: Zuideman labeled dietary factors as an additional etiologic agent and proposed that the entity known as "tropical pancreatitis" in underdeveloped countries was associated with standard low protein and fat-deficient diets prevalent in some areas in the world

The increase in the diagnosis of chronic pancreatitis in recent years probably reflects a wide variety of factors including increased awareness, greater diagnostic skills and more sophisticated technology, as well as an increase in alcohol consumption.[17]

Factors that may increase the risk of chronic pancreatitis that have been published in medical literature include:

> Gender: males

> Age: late teens to mid-twenties (for hereditary cases)

> Age: over 50 (for cases of no known cause)

> Heavy alcohol consumption

> Smoking

> Family history of hyperparathyroidism associated with chronic pancreatitis

> Race: African-Americans

d. Classification of Chronic Pancreatitis

The first classification system is the **TIGAR-O** Classification System. The TIGAR-O (**T**oxic/Metabolic, **I**diopathic, **G**enetic, **A**utoimmune, **R**ecurrent/Severe Acute Pancreatitis, **O**bstructive) classification system is based on risk factors for chronic pancreatitis.

Toxic – metabolic

> Hypercalcaemia

> Hyperlipidaemia

> Chronic renal failure

> Drugs

> Toxins (alcohol and smoking)

Idiopathic (the cause of pancreatitis is unknown)

Genetic

> Gene mutations

Autoimmune

> Sjogren's syndrome

> Inflammatory bowel disease (IBD)

> Primary biliary cirrhosis (PBC)

> Recurrent acute pancreatitis

Obstructive

> Pancreas divisum

> Sphincter of Oddi dysfunction

> Duct obstruction (stones, post-inflammatory, posttraumatic)

The second classification system used to identify pancreatitis is the **SAPE** system- **S**entinel **A**cute **P**ancreatitis **E**vent. David C. Whitcomb, MD described the SAPE hypothesis model as:

"The new model is the Sentinel Acute Pancreatitis Event (SAPE) hypothesis model. This model organizes factors associated with chronic pancreatitis according to a hypothetical pathway that leads from an episode of acute pancreatitis towards chronic pancreatitis. In this model, the first (or sentinel) episode of acute pancreatitis recruits and activates the immune cells and stellate cells that are crucial for the development of chronic inflammation and fibrosis. Thus, the SAPE hypothesis model identifies a point in time when various risk factors (e.g. alcohol consumption and smoking) become etiologic factors, and initiate the process that ends in chronic pancreatitis. Furthermore, the origin and mechanism of complications such as pain and diabetes can be assessed. Organizing, quantifying and sequentially categorizing these factors will be vital for understanding chronic pancreatitis as a group of mechanisms and pathways rather than as an end-stage pathologic scar, and for defining specific risk, pathways and treatment opportunities for individual patients."[12]

The SAPE hypothesis focuses on missing the functional stage of developing chronic pancreatitis. In many cases the acute pancreatic event may be subclinical and patients do not seek medical attention at all. Without proper medical care in the early stages these patients within 5-15 years will develop the final stage of the chronic pancreatitis as it is described now in medical literature with constant pain, steatorrhea (fat in the stool) and malabsorption (indigestion of food).

A few thoughts about **Biotherapy Clinical Functional Classification**

The authors consider that chronic pancreatitis, like all the chronic inflammation and degenerative diseases, has three stages: functional stage, destructive stage and final failure stage of the process. In all of these stages, there are different degrees of exocrine pancreatic deficiency.

To help primary care physicians and medical practitioners postpone the development of the final failure stage of chronic pancreatitis, the authors offer their *Biotherapy Clinical Functional Classification of Exocrine Pancreatic Deficiency* diseases, which focuses on the early stages of this illness.

1. ***Acidic pancreas and bile***

2. ***Pancreatic deficiency***

3. ***Pancreatic failure***

By analogy with chronic inflammation diseases of other inner solid organs, chronic pancreatitis is initiated either from an acute event or develops slowly without a clearly identified time when the process started. It can be a functional condition with minimal, vague digestive symptoms and almost normal clinical tests. Apparently, this could be one of the reasons that patients do not seek medical care in the early stage of chronic pancreatitis.

All organs and systems have functional capacities. Typically, the organism employs just part of the organ capacity. Only in extreme situations, such as survival, does the organ require 100% capacity of the function.

To simplify, the functional capacity means how much organ's function may be gone, but the organ can function at the level to keep the organism survive. For example, two kidneys have 75% functional capacity, the liver has 65% functional capacity, and the lungs have 50% functional capacity. It presumes that 25% kidney tissue, or 35% liver tissue or 50% of lung tissue can be left functional to keep the human organism alive.

The pancreas has 90 % functional capacity, much more than other solid internal organs. For the pancreas it presumes that symptoms and tests begin displaying serious abnormalities after only 10% pancreatic functional capacity is left. Enormous pancreatic functional capacity is good for the human organism but this causes many difficulties to diagnose the chronic pancreatitis in the early stage.

Continuing the analogy with other solid internal organs, the processes of their inflammations also have three stages: the functional stage, destructive stage and final decomposing stage - failure of the organ.

These disorders and diseases are well described for the liver, lungs, kidneys, and heart but not for the pancreas.

Functional Stage => => => => Destructive Stage => =>=> => Failure of the Organ

Reversible Stage---------- Partial Reversible Stage---------- Final/ Degenerate Stage

Chronic hepatitis => =>=> => Liver fibrosis => =>=> => => => Liver failure

Chronic pneumonia => => => Pneumosclerosis (fibrosis) => => Respiratory (lung) failure

Chronic nephritis => => => =>Nephrosclerosis (fibrosis) => => Kidney failure

Chronic miocardytis => => => Miocardiosclerosis (fibrosis) => Heart failure

All stages of chronic inflammation of solid inner organs typically have diagnostic criteria along with conventional and alternative medicine treatments.

How about the pancreas? Most medical books describe chronic pancreatitis from its final stage – *pancreatic failure*. Something is wrong with this picture therefore, the authors attempt to fill the vacuum by helping medical providers to focus on the early stages of chronic pancreatitis.

Chronic pancreatitis is similar to other chronic inflammatory diseases such as chronic kidney, lung, liver, and heart inflammation. All chronic inflammation diseases cause the progressive damage and destruction of organs and replace normal tissue with scarring tissue (fibrosis) while losing organ functions. In case of the pancreas, it is the loss of exocrine and endocrine functions that generally loses production of digestive enzymes and insulin.

Biotherapy Clinical Functional Classification of Exocrine Pancreatic Deficiency may be a simple tool to help medical providers to clinically diagnose, treat, and improve the quality of life for many sufferers from pancreatic (digestive) diseases. So, the lists above can be continued as:

Functional Stage => => => => =>Destructive Stage => =>=> => Failure of the Organ

Chronic pancreatitis => => => => Pancreatic fibrosis => =>=> => Pancreatic failure

Acidic pancreas and bile*=> => => *Pancreatic deficiency* => =>=> *Pancreas failure

e. Signs and Symptoms of Chronic Pancreatitis

Biotherapy Clinical Functional Classification of Exocrine Pancreatic Deficiency uses the clinical symptoms to differentiate the stages of the chronic pancreatitis.

Chronic pancreatitis may be asymptomatic over extended periods of time. It usually takes several years (approximately from 8 to 15 years) for permanent changes in the pancreas and the diagnosis is established. The average time from the onset of symptoms until the diagnosis of chronic pancreatitis is 62 months, add or subtract 4 months. The delay in diagnosis is even longer in people without alcoholism, in whom the average time is 81 months from onset of symptoms to diagnosis.[15]

The symptoms of chronic pancreatitis from medical literature are similar to the *pancreatic failure* stage. The main symptoms are chronic pain, weight loss, and manifestations related to the loss of functional pancreatic tissue such as malabsorption and diabetes. Malabsorption is the difficulty digesting or absorbing nutrients from food.

i. Pain

The primary ongoing symptom of chronic pancreatitis is pain localized at the upper abdomen that often radiates to the back. Episodes of pain last from hours to days, and may eventually become continuous. Eating may worsen the pain. Abdominal pain is responsible for most hospitalizations related to this illness.

Clinically, the patient experiences intermittent attacks of severe pain, often in the mid or left upper abdomen and occasionally radiating to the mid back. The pain may occur either after meals or independently of meals, but it is not fleeting or transient and tends to last at least several hours. During an attack, patients may assume a characteristic position in an attempt to relieve their abdominal pain (lying on the left side, flexing the spine and drawing the knees up toward the chest).

The history of pain in chronic pancreatitis is highly variable. Most patients experience intermittent attacks of pain at unpredictable intervals, while a minority of patients experience chronic pain. In some patients, pain severity either decreases or resolves over 5-25 years. Nevertheless, ignoring pain relief with the expectation that the disease eventually will resolve itself is inappropriate.

In alcohol-induced diseases, eventual cessation of alcohol intake may reduce the severity of pain. The variability in the pain pattern contributes to the delay in diagnosis and makes determining the effect of any therapeutic intervention difficult. Small percentages of patients (20%) have painless chronic pancreatitis and present with signs or symptoms of pancreatic exocrine or endocrine deficiency.[15]

ii. Exocrine Pancreatic Deficiency

Gradual pancreatic fibrosis produces a steady deterioration in enzyme output, leading to steatorrhea and weight loss. Steatorrhea is the presence of excess fat in feces. Stools may also float due to excess lipids, have an oily appearance, and be especially foul smelling. An oily anal leakage or some level of fecal incontinence may occur. However, clinically apparent steatorrhea does not occur until 90% of pancreatic function has been lost.

Losing weight may be due to the fear of exacerbation of pain after eating, lower appetite, nausea, vomiting, pancreatic exocrine deficiency (malabsorption or maldigestion) and constant loose stool - steatorrhea. The sudden development of steatorrhea may suggest main pancreatic duct obstruction by inflammatory strictures or possibly even cancer.

The severe consequence of maldigestion (impaired digestion) leads to muscle wasting and deficiencies in fat-soluble vitamins (A, D, E, and K). A common complication of pancreatitis is cobalamin (vitamin B12) deficiency.

iii. Endocrine Pancreatic Deficiency/Diabetes

Diabetes does not occur until late in the pancreatitis course. It is also possible that some of the diabetics are actually patients with chronic pancreatitis. However, the diagnosis of chronic pancreatitis might be missed in clinical practice because the symptoms of exocrine pancreatic deficiency are not specific in the early stages of chronic pancreatitis. On the other hand, the prevalence of diabetes mellitus in chronic pancreatitis is 40-70%, and in chronic-calcifying pancreatitis up to 90%.[54]

More information can be found in the chapter 16-*The Role of Exocrine Pancreatic Deficiency in Metabolic Syndrome, Obesity and Diabetes.*

f. Chronic Pancreatitis Complications

Incidence of the various complications of the acute or recurrent pancreatitis:

> Chronic pain 80% to 90%

> Diabetes mellitus > 40%

> Weight loss> 40%

> Pancreatic cancer 15% to 40%

> Pseudocyst25% to 30%

> Malabsorption and steatorrhea 10% to 15%

> Bile duct, duodenal, or gastric obstruction 5% to 10%

> Pancreatic ascites or pleural effusion< 10%

This information has been adapted from the article *Chronic pancreatitis*, by Nair RJ *et al*. and was originally published in a 2007 edition of *American Family Physician*.[117]

g. What are the Consequences of Chronic Pancreatitis?

The main problem for patients with pancreatitis is reduced physical and emotional qualities of life through:

> General pain, pancreatic pain, insomnia, fatigue, chronic diarrhea, low body weight and loss of sexual function

> Fear of future health problems, hospitalization, unemployment, financial burden and a disrupted social life leading to depression and thoughts of suicide

> Narcotic dependency, if narcotics are required for pain

Morbidity and mortality are typically caused by debilitating pain, progression to diabetes, and pancreatic cancer, leading to mortality being caused mainly by cardiovascular events and sepsis. Most patients will develop diabetes, with the onset about five years after the initial diagnosis. There is a 15-fold risk of pancreatic cancer for patients with chronic pancreatitis who are alcoholics.

Interesting facts at a glance:

Chronic pancreatitis (CP) is the gradual progression of pancreatic inflammation, which causes permanent tissue damage and the gradual replacement of healthy pancreatic tissue with scar tissue (fibrosis).The following three factors may be indicative of chronic pancreatitis: recurrent injury, persistent inflammation, and significant anti-inflammatory response (fibrosis)

Diets, lifestyles and environmental chemicals have a huge impact on the development of acute and chronic pancreatitis

Other factors may increase the risk of chronic pancreatitis such as gender, age, heavy alcohol consumption, smoking, race, etc

Specialists hold equally divergent views as to the diagnostic and conventional treatments for pancreatitis. Biotherapy Clinical Functional Classification of Exocrine Pancreatic Deficiency may be a simple tool to help medical providers evaluate and improve the quality of life for many sufferers of pancreatic (digestive) diseases. This classification describes symptoms according to the stage of the process

Symptoms of chronic pancreatitis mainly depend upon inflammation (pain), exocrine pancreatic deficiency (malabsorption, steatorrhea, nutritional deficiencies, weight loss) and endocrine pancreatic deficiency (diabetes)

Chronic pancreatitis is a progressive debilitating disease with many complications and reduced physical and emotional qualities of life

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Chapter 11-Alcoholic Pancreatitis

For individuals lacking a medical background

Many individuals with alcohol abuse don't think about consequences of heavy alcohol consumption until suddenly they are struck by an attack of acute abdominal pain, nausea, vomiting and fever. Doctors from the hospital ICU confirm the diagnosis of acute pancreatitis, save the patient's life (mortality in this condition is about 10%), and the happy survivor is discharged with strict recommendations to quit alcohol.

There are two problems going on here.

1. How to stop drinking?

2. What will happen to the pancreas after an attack of acute pancreatitis?

First, after heavy drinking for extended periods of time, quitting alcohol is a serious problem for everyone. In our clinical experience, this is almost impossible without help from a knowledgeable licensed practitioner or even a team of practitioners.

Second, the first attack of alcoholic pancreatitis usually leads to chronic pancreatitis with serious decreasing of the quality of life and life span. Pancreatic cancer often follows chronic alcoholic pancreatitis. Now, if individuals are lucky enough to be discharged from the hospital and stop drinking alcohol, they have to recover from the damage alcohol made to their pancreas to prevent future attacks of pancreatitis.

Acute pancreatitis affects 80,000 to 200,000 people in the U.S. annually. Moreover, these numbers are getting higher year by year. Gallbladder, liver diseases, and alcohol abuse are major risk factors for pancreatitis. 80% of acute pancreatitis cases are developed from these conditions. Not all alcoholics finish their life with pancreatitis. Nevertheless, after the pancreatic attack, alcohol becomes a dangerous toxic substance for the pancreas at any quantity and types (hard liquor, wine, and beer).

There is not a safe dose of alcohol after an attack of pancreatitis; the life span really depends on consumption of alcohol

This has been proven by scientific research. Approximately 5 to 6 years after the onset of the disease, patients who continue to drink will develop full-blown chronic pancreatitis as a result of progressive destruction of the pancreatic gland.

The harmful actions of alcohol on the pancreas are very complicated and depend on "how much" and "how long" and "what kind" and can be divided on the toxic effect of alcohol on the nervous system and influence on the digestive hormones and direct action of alcohol on the pancreas.

Alcohol induces pancreatitis by causing small pancreatic ducts to be blocked by protein plugs. It is known that alcohol inhibits the secretion of pancreatic juice and decreases the amount of protein, bicarbonate, minerals and trace elements. Next, alcohol literally kills the pancreatic cells and causes self-digestion of the pancreas by its own pancreatic enzymes.

Even small doses of alcohol induce spasms of the Sphincter of Oddi, leading to a backup of pancreatic enzymes inside the pancreas. The pancreatic digestive enzymes, which collected inside, start to digest their own pancreatic cells. It causes congestion, inflammation, pain, cysts and finally death of the pancreatic gland tissue.

Moreover, alcohol by itself produces severe acidity in the body. This can be easily checked by anyone. First, check the pH of saliva and urine by litmus paper and then drink a bottle of beer. Second, after 40 minutes, check the pH again. The result will be obvious: the litmus paper will turn more yellow (entering the body acidic stage). Thus, if alcohol is often consumed, the saliva and urine will always be acidic (pH less than 6.6).

Too many acid radicals make chaos in whole body's metabolism causing deposits of proteins, fats and calcium directly into the pancreas (fatty pancreas, pancreatic calcium stones), which shut down pancreatic function and whole digestion. Acidity stops the action of pancreatic digestive enzymes. This results in the lack of many vital nutrients because the organism cannot digest them from food. This is why alcoholics suffer from a deficiency of vitamins, essential fatty acids, amino acids, many minerals, and trace elements.

In a nutshell, it is VERY important for patients to stop drinking alcohol once and for all. But how? Some individuals can give up drinking alcohol with no problem whatsoever. However, it is incredibly hard for many individuals to stop drinking completely. Actually, many experts feel it is next to impossible to completely overcome alcohol addiction without the assistance of an experienced licensed practitioner or even a team of licensed specialists.

Another hurdle facing patients and their families is the inability of the sick person to admit that they have an alcohol problem. Sometimes it helps to assess honestly the alcohol consumption in your life. Try taking the test below, and see if you might have a problem with alcohol.

Personal Alcohol Assessment Test

Answer the questions below to see if you have alcohol issues. Answer honestly, because nobody will see the answers but you:

*** Do you ever feel like you drink too much?**

*** Do others disapprove of the amount of alcohol that you drink?**

*** Do you find it hard to stop drinking after a drink or two?**

*** Do you ever feel guilty or secretive about drinking?**

*** Do you have to have a drink right after you wake up as a remedy for hangover or to calm your jitters?**

*** Have you ever blacked out while you were out drinking?**

*** Has drinking caused you problems with your relationships, health, or job? Has it ever caused you problems with the law?**

Test results reveal that one "yes" answer could mean a problem with alcohol. Two "yes" answers show a high probability of alcohol addiction. In either case, you should make an appointment as soon as possible to discuss the test results with an experienced and licensed practitioner. They will be able to help you map out a custom treatment plan.

If a patient who has had an attack of acute pancreatitis is able to stop drinking, then there is a good chance that his/her pancreas will heal. This will prevent future attacks of pancreatitis. Don't lose the time!

"The time to repair the roof is when the sun is shining". ***John F. Kennedy***

For individuals with a medical background

Many studies show that in Western countries alcohol is the most frequent associated factor of chronic pancreatitis (50-80% of cases).

Alcoholic Pancreatitis is a potentially fatal inflammation of the pancreas associated with continuous alcohol consumption. N. Friedreich reported a connection between alcohol abuse and pancreatic damage as early as in 1878.[1]

Alcoholic pancreatitis is a possible deadly disease that may be acute or chronic. In severe acute pancreatitis cases, the risk of death rises to about 30 percent.[2]

a. Males vs. Females

Alcoholic chronic pancreatitis presented clinically in young male adults (30-40 years of age) give the idea for some doctors to refer to this condition as “male pancreatitis”. Unfortunately, consumption of alcohol by women has been on the rise for decades, which makes the gender differences less obvious. In many situations, histological (by microscope) lesions were chronic from beginning of the alcoholic pancreatitis and this disease was characterized by recurrent attacks of abdominal pain.[21]

There is solid evidence that indicates the existence of a link between the amount of alcohol consumption and the risk of pancreatitis. Irving HM *et al*. (2009) found, in six studies focusing on 146,517 individuals with 1,671 cases of pancreatitis, the dependence on the dose-response relationship between an average volume of alcohol consumption and pancreatitis. Those with a daily alcohol intake of 96 grams, or eight standard drinks, had a four-fold increased risk of pancreatitis relative to non-drinkers.[22]

The Dietary Guidelines for Americans, published by the U.S. Departments of Agriculture and Health and Human Services, define a standard drink of alcohol as "12 ounces of regular beer, 5 ounces of wine, or 1.5 ounces of 80-proof distilled spirits." All of which contain the same amount of alcohol.

The minimum amount of alcohol necessary for the appearance of chronic pancreatitis has not been clearly established; it is however considered that even a relatively moderate level of alcohol intake (40-50 g of pure alcohol per day) can cause chronic pancreatitis.[21]

The average duration of alcohol consumption before the onset of pancreatic symptoms is 18 (plus - minus 11 years) for males and 11 (plus - minus 8 years) for females.

Because of several physiological reasons, females will feel the effects of alcohol more than males, even if they are the same physical size. There is also increasing evidence that females are more susceptible to damaging effects of alcohol than males. Researchers offer what appears to be the answer: females have far smaller quantities of alcohol dehydrogenase - the protective enzyme that breaks down alcohol in the liver.

Experts believe this lack of protection may help explain why alcoholic females suffer more heavily from liver and pancreas damage than do alcoholic males.

b. Research

As far as the role of alcohol in development of pancreatitis is concerned, many authors who studied chronic pancreatitis in various countries confirmed this information.

Alcohol is the leading factor of chronic pancreatitis in many countries.[21, 24]

Australia 95%

Brazil 90%

France 77%-88%

Italy 75%-78%

Korea 64%

South Africa 67%

Switzerland 69%-71%

United States 75%

The mortality rate of patients with alcoholic pancreatitis is about 36 percent higher than that of the general population.

Lucio Gullo (2005) stated in his paper *Alcohol and Chronic Pancreatitis: Leading or Secondary Etiopathogenetic Role,* "Approximately 50 percent of patients with alcoholic pancreatitis die within 20 years of onset of the disease."[21] The increased risk of pancreatic cancer is heavily reported in abusive alcohol users. One complicating factor is cigarette smoking, which is commonly associated with alcohol abuse.

Many researchers agree that the mechanism by which alcohol causes chronic pancreatitis today is not known.[21] Chronic alcoholic pancreatitis has many more questions than clear answers. Alcohol research depends essentially on animal models because controlled experimental studies of ethanol-induced diseases in humans are unethical. However, the ideal animal model for chronic alcoholic pancreatitis does not yet exist.[98]

Epidemiological studies and animal experiments suggest that alcohol, by itself, is not sufficient to induce the disease. In fact, less than 10 percent of heavy alcohol users (180 g/day or about 15 drinks/day for 10 - 15 years) eventually develop clinically obvious alcoholic pancreatitis.

Ammann R.W. (2001) published the article *The natural history of alcoholic chronic pancreatitis* in *Internal Medicine*. He wrote "Researchers have analyzed several other predisposing factors, such as the amount and pattern of drinking, smoking, dietary habits, and genetic mutations - particularly those of alcohol-metabolizing enzymes, but none of these factors has been firmly linked to the development of alcoholic chronic pancreatitis ".[90]

It generally recognizes that alcoholic pancreatitis begins as a chronic disease with occasional episodes, or acute "flare-ups". This idea was based on results of tissue analyses and X-ray studies taken from alcoholics during their first attack of pancreatitis that seemed to reveal signs of already existing chronic pancreatitis. Among these signs were shrinkage of tissue (atrophy), replacement of healthy tissue by scar tissue (fibrosis), and hardening of tissue caused by calcium deposits (calcification). Furthermore, Vonlaufen A*, et al.* wrote in their article *Role of alcohol*

metabolism in chronic pancreatitis, that autopsy studies demonstrated evidence of pancreatic fibrosis in alcoholics who had no history of clinical pancreatitis. It now is generally accepted that acute and chronic alcoholic pancreatitis is the same disease at different stages.[91]

According to the article *Alcohol as a risk factor for pancreatitis. A systematic review and meta-analysis* by Irving H M *et al*., 46% of patients with acute alcoholic pancreatitis had recurrent attacks within 10-20 years, with 30% having a recurrence during the first 3 years.[22]

In a large prospective study of Ammann R.W *et al*. (1994), changes in the pancreas related to chronic pancreatitis were more likely to occur in alcoholics who had recurrent acute inflammation of the pancreas.[92]

Experiments also showed that repeated episodes of acute pancreatitis in rats produced chronic changes in the pancreas, including fat deposits, atrophy, and fibrosis. [23]

c. Harmful Effects of Alcohol on the Pancreas

Alcohol abuse can cause repeated episodes of pancreatic tissue inflammation. This constant damage can lead to death of pancreatic cells, scarring of pancreatic tissue (extensive fibrosis) and obstruction of the pancreatic ducts, thus leading to pancreatic failure.

The harmful action of alcohol on the pancreas is very complicated and involves several different factors.

Possible mechanisms of developing pancreatic damages by alcohol abuse include:

- Sphincter of Oddi Dysfunction
- Changing of pancreatic fluid to favor the formation of protein plugs and stones
- Direct toxic effects of alcohol on acinar cells
- Effect of alcohol on pancreatic digestive enzymes
- Effects of toxic acidic metabolites of alcohol
- Problems for absorption and excretion of other nutrients
- Reducing pancreatic microcirculation after alcohol consumption
- Decreasing pancreatic hemoglobin oxygen saturation

As a strong narcotic, alcohol has dual action on the nervous system. In small doses, alcohol activates the nervous system and in large doses alcohol oppresses the function of the nervous system. The first small doses of alcohol stimulate the appetite and pancreatic secretion. On the other hand, consumption of large doses may shut down the pancreas.

Alcohol causes either spasms or flabbiness of the smooth muscles in the Sphincter of Oddi. Spasms can cause back up of bile and pancreatic juice, bile reflux and activation of pancreatic enzymes inside the pancreas. Some researchers consider that backflow of bile or the contents of the duodenum into the pancreatic duct also lead to pancreatic damage.

In addition, alcohol influences the autonomic nervous system negatively, thus causing chaos in proper releasing and work of digestive hormones – the main regulators and conductors of upper gastro intestinal tract function.

Alcohol and its very acidic metabolites cause serious damage to the pancreas

This idea it is not new one. In 1988, Claus Niederau and James H. Grendellin in *The Journal of Glinical Investigation* stated that acidification may play a role in the development of acute pancreatitis.[228]

Bhoomagoud M *et al*. (2009) from the Department of Internal Medicine at Yale University School of Medicine, New Haven, Connecticut, USA, suggested that metabolic acidosis may be the risk factor for developing pancreatitis. Those authors experimentally in vivo and in vitro found that reducing pH (acidification) increased the sensitivity of the acinar cells to zymogen activation.[229]

Alcoholics typically suffer from severe metabolic acidosis.

It is the opinion of the authors, that the combination of whole body acidity with direct toxic influences of alcohol and its acidic metabolites on the pancreatic cells are the key to understanding the prevalence of pancreatitis after alcohol consumption.

It is known that tissue acidity decreases hemoglobin oxygen saturation.

In their book, *Alcohol and the Gastrointestinal Tract*, Singer MV and Brenner DA wrote about the state of decreased hemoglobin oxygen saturation continuing in the pancreas one hour after alcohol consumption. [98] This is can be a possible link between acidity, pancreatic tissue hypoxia and specific pancreatic damage.

As an osmotic diuretic, alcohol drains water, minerals, trace elements, bicarbonate and water-soluble vitamins from the body. These deficiencies change the biochemistry and biomechanical properties of the bile and pancreatic juice. “Aggressive” acidic bile mixed with pancreatic juice burns and erodes the walls of the bile duct, Sphincter of Oddi, and the duodenum. In its turn, this causes the irritation, inflammation, and spasms of smooth muscles in those areas.

Most alcohol abusers suffer from Sphincter of Oddi Dysfunction, which can manifest by abdominal cramps or pain, abdominal distention, nausea, vomiting, diarrhea or loose stool, belching and heartburn mostly after an alcohol binge, but may be also after everyday drinking.

Even one attack of Sphincter of Oddi pain after alcohol intake is an alarming bell of developing of pancreatic or/and gallbladder disorders leading to possible pancreatitis in the near future.

Pancreatic injury that is caused by alcohol induced spasms of the Sphincter of Oddi, leads to a backup of pancreatic enzymes into the unprotected tissues of the pancreas. Therefore, instead of entering the intestine to digest food, the enzymes "digest" the pancreatic cells themselves.

Nevertheless, alcohol has a direct harmful impact on the pancreas in many ways. For example, Singer MV, Brenner DA in their book "*Alcohol and the gastrointestinal tract*" mentioned that after alcohol administration, pancreatic microcirculation in the animals was diminished.[98]

d. Alcohol and Pancreatic Enzymes

Most recent research into how the alcoholic pancreatitis develops fixes attention on the direct toxic effects of alcohol on acinar cells. Acinar cells produce large amounts of digestive enzymes, which have the possibility to cause pancreatic cell injury during their premature activating inside the pancreas. A single pancreatic acinar cell can synthesize and secrete up to 10 million molecules of enzymes per day. The acinar cells are normally protected from digesting themselves by:

> manufacturing digestive enzymes in inactive forms (zymogens)

> segregating zymogens within membranous compartments (zymogen granules)

> producing protective enzymes (trypsin inhibitors) that destroy active digestive enzymes

Any disruption of these normal protective mechanisms by alcohol could result in premature activation of zymogens and subsequent "autodigestive" pancreatic injury. If pancreatic digestive enzymes start to digest their own pancreas, pancreatitis develops.

Long-term alcohol consumption may lead to premature activation of digestive enzymes in the acinar cell. In this regard, it has been shown that alcohol decreases the production of digestive enzymes in the pancreas [93] and increases the fragility of the zymogen granules[94], potentially allowing zymogens to leak into the cell and damage them.[23]

When alcohol is consumed, it passes from the stomach and intestines into the blood, a process referred to as alcohol absorption. Liver enzymes, especially alcohol dehydrogenase, metabolize alcohol to acetaldehyde. Ethanol and its metabolites, specifically acetaldehyde, are primarily responsible for much of the cellular damage associated with alcohol consumption.

In normal conditions, a small amount of alcohol is metabolized in the pancreas, as it is in the liver, via alcohol dehydrogenase to acetaldehyde. Acetaldehyde is a highly reactive, carcinogenic and very toxic acidic compound. Therefore, excess of acetaldehyde can have direct pathological effects on the pancreatic cells, as it occurs in the liver.

Two other acidic toxic metabolites of alcohol, known to accumulate in the pancreas after chronic alcohol consumption are cholesteryl esters and fatty acid ethyl esters (FAEE's).

e. Alcohol and Candida

There is an obvious link between alcohol addiction and dysbiosis (Candida-yeast overgrowth). Alcohol and its toxic metabolites, by reducing antimicrobial quality of pancreatic juice, decrease direct harmful action on unfriendly intestinal flora, thus causing Candida-yeast overgrowth.

On the other hand, Candida-yeast causes inner fermentation by manufacturing not only ethyl alcohol but also other even more toxic alcohols such as methyl alcohol. Alcoholics with chronic pancreatitis undergo many rounds of antibiotics that cause chaos in internal ecology with possible Candida-yeast overgrowth, as well.

Candida is a common pancreatic infection. For example, according to Aloia T *et al*. (1994) from the Department of Surgery, UCLA Center for Health Sciences, USA, 41% of patients were Candida infected.[230]

There is considerable evidence that Candida-yeast, by fermentation, produces additional alcohol and its by-products: acetaldehyde, n-propanol, lactic acid, hydrogen, acetone, etc.

In case of intestinal yeast overgrowth and inner fermentation, alcohol enters the bloodstream and the levels of alcohol in the blood are increased. From London, England, Hunnisett A *et al*. (1990) described "Auto Brewery Syndrome". Chronically sick individuals were tested for blood ethanol levels an hour after absorbing a sugar solution. These patients constantly had high blood levels of ethanol, that the researchers considered came from intestinal yeast overgrowth.[159]

Individuals with Candida-yeast overgrowth constantly produce their own alcohol. They may as well be walking brewery factories.

Yajima D *et al.* (2006) first discovered "Drunk disease" in Japan. These researchers found alcohol in the blood of individuals with chronic candidiasis even when they did not drink any alcohol. What's more, the Japanese researchers found that ethanol concentrations in blood samples taken after death were increased in individuals with candidiasis.[156]

f. Alcohol and Pancreatitis

A history of excessive alcohol consumption is found in the majority of patients with chronic pancreatitis, and many research efforts revealed insights into the alcohol induced pancreatic damage. However, according to experts in alcoholic pancreatitis, Schneider A, Singer MV.

(2005) “the exact mechanisms underlying the disease are not yet clarified, and the origin of alcoholic chronic pancreatitis continues to be the topic of speculation and investigation”.[99]

The fact that only 10% of heavy drinkers develop pancreatitis has stimulated an intensive search for trigger factors, which may lead to a pancreatic attack. Susceptible factors examined so far include diet, smoking, amount, and type of consumed alcohol, the pattern of drinking, fat intolerance and a range of genetic factors. Disappointingly, despite this research, no clear association has been established between the above factors and alcoholic pancreatitis.

There is evidence that the development of alcoholic pancreatitis has a multifactor nature. The authors speculate that the most important triggers of developing alcoholic pancreatitis have an interrelated direct harmful action of alcohol on the pancreas that is aggravated by systemic and pancreatic metabolic acidosis and intestinal dysbiosis.

Working for many years with alcoholics, the authors often could see development of acute pancreatitis after an alcohol binge. Typically, heavy drinking throughout the days or even weeks, leads to dehydration, vomiting and the cessation of food intake for more than 24 hours. In many situations, alcohol binging can cause ketoacidosis and lactoacidosis – the rigorous acidic conditions. Severe metabolic disorders with a deficiency of vital minerals, trace elements, vitamins, and bicarbonates cause problems with microcirculation, thus, potentially resulting in inner toxicity. During this period of starvation, vomiting continues, and abdominal pain develops, leading the patient to seek medical attention. Very often, tests revealed elevation of pancreatic enzymes in the blood and other signs and symptoms of pancreatic damage.

g. Alcohol and Acidity

Alcohol is a strong acid productive agent causing the whole body to become acidic – chronic metabolic acidosis. Besides the very complicated invasive tests of the pancreatic juice, shifting the body’ fluids, blood tests, etc., the chronic acidic condition may be verified by simple regular testing of saliva and urine pH to quantify this condition and treatment effectiveness.

We usually see positive clinical changes between cessation of drinking and GI symptoms. Our experience shows that these positive clinical changes also correlate very well with less acidity (increasing pH) of saliva and urine of those with alcohol abstinence.

While alcohol consumption is considered a key factor associated with pancreatitis, alcohol alone does not cause acute and chronic pancreatitis.

There are some factors that trigger toxic effects of alcohol on the pancreas and lead to chronic pancreatitis. The authors suppose that one of the causative factors that promote the alcohol – pancreas damage is metabolic acidosis.

The development of acute and chronic alcoholic pancreatitis is triggered by metabolic acidosis and consequent harmful changes in biochemistry of pancreatic juice and bile

h. Alcohol and Toxicity

There is evidence that a high intake of alcohol promotes protein alteration in the pancreatic juice and this is one of the harmful consequences of the toxic effects of excessive alcohol intake on acinar cells. Researchers hypothesized that alcohol induces pancreatitis by causing small pancreatic ducts to be blocked by protein plugs, and these plugs enlarge and calcify.

Substantial evidence supports a role for active digestive enzymes, such as trypsin, in pancreatic injury. Perhaps the most compelling evidence that activation of trypsin plays a role in pancreatitis, is the recent discovery of Whitcomb DC *et al*. (1996) [95] of a mutant gene in patients with hereditary pancreatitis.[95]

"This mutation produces a trypsin variant that cannot be degraded by the acinar cell's protective enzymes. The accumulation of active trypsin could initiate activation of other enzymes, resulting in the autodigestion of the pancreas" by Minoti V, Apte MV in "Alcohol-Related Pancreatic Damage. Mechanisms and Treatment". http://pubs.niaaa.nih.gov/publications/arh21-1/13.pdf [23]

In addition to alcohol, a role in the development of chronic pancreatitis can be played by genetic predisposition. Various studies have been carried out in recent years, which emphasize the role of these factors in alcoholic pancreatitis. Hereditary factors may play the role but only in 2-4% of chronic pancreatitis cases. The first attack of heredity pancreatitis typically occurs within the first two decades of life when the regular alcohol consumption usually is not a large problem yet. In the United States, it is estimated that at least 1,000 individuals are affected with hereditary pancreatitis. [107] The major role belongs to environmental factors, which can cause gene mutation of pancreatic enzymes to promote their activation inside the pancreas.

Clinical paradoxes exist with incidences of pancreatitis in alcoholics. Although it is a well-known fact that the risk of developing pancreatitis gets higher with increasing alcohol consumption, it is also evident that only a small proportion of heavy drinkers develop pancreatitis (about 10%).

i. Environmental Factors and Life Style

Environmental factors that influence the susceptibility of pancreatitis include the amount and type of alcohol consumed, the pattern of alcohol consumption, hereditary factors, fat intolerance,

etc. In addition to alcohol, a few other factors have been considered to have a role in the development of alcoholic chronic pancreatitis; diets and smoking.

The study of Sarles H (1973) showed that a diet rich in protein and fat may play a role in the causing of alcoholic chronic pancreatitis.[97] Before the development of chronic pancreatitis, individuals were big eaters and heavy drinkers. A high concentration of proteins in pancreatic juice is one of the first changes in the alcoholic chronic pancreatitis. Thus, some researchers hypothesize that an excess of proteins and fats in the diet can play a role in the onset of high concentration of proteins in the pancreatic juice and this can be provoked through an increased release of hormones, such as cholecystokinin, which stimulate pancreatic protein secretion.

Smoking is focused on for its possible role in the development of alcoholic chronic pancreatitis, as well. In reality, almost all the patients with alcoholic pancreatitis are also heavy smokers. [108] However, the mechanism by which this can occur is not known. Most authors believe that if smoking does play a role in the etiology of alcoholic chronic pancreatitis, then it is certainly secondary as compared to the role of alcohol.

Evidence of chronic pancreatic disease develops as a result of the progressive destruction of pancreatic tissue. Patients seek medical attention for persistent pain (which often leads to narcotic addiction from the excessive use of pain medication), weight loss, diabetes, and maldigestion of food (a result of inadequate production of digestive enzymes by the pancreas). [23] As a really toxic agent for the liver and pancreas, alcohol speeds up these disorders. After approximately 8-15 years, most individuals who abuse alcohol or are heavy habitual drinkers have their symptoms altered. The symptoms worsen and the structural changes in the stomach, liver, gallbladder, pancreas, and duodenum appear. Even the moderate regular consumption of alcohol with “binge drinking” is significantly associated with diseases of the gastrointestinal tract. In Europe and the USA, more than 20% of men and approximately 9% of women hospitalized in varying medical departments in general hospitals feature alcohol related disorders.[98]

j. Who Is an Alcoholic and How Does Alcoholism Develop?

According to the National Institute on Alcohol Abuse and Alcoholism (NIAAA), 14 million Americans are alcoholics and a few million drink large amounts regularly and are good candidates to become alcoholics. According to alcohol dependence studies, more than half of U.S. alcoholics are young people, averaging 24 – 26 years of age.[25]

Drinking continues to be widespread among adolescents, as shown by nationwide surveys as well as studies in smaller populations. According to an annual survey of American youth, three-fourths of 12th graders, more than two-thirds of 10th graders, and about two in every five 8th

graders have consumed alcohol. The survey is titled *Monitoring the Future* (MTF) and can be found online at http://monitoringthefuture.org/pubs/monographs/vol1_2005.pdf.

In 2005, 29% of 12th graders had engaged in heavy episodic, or binge drinking. The NIAAA defines binge drinking as a pattern of drinking alcohol that brings blood alcohol concentration [BAC] to 0.08 grams % or higher. For the typical adult, this pattern corresponds to consuming five or more drinks for men or four or more drinks for women in about 2 hours.

To put into account the scientific data above, out of 14 million alcoholics, half of them are young (close to age 25) and have not yet developed problems with digestion and a low function of the pancreas. If they continue to drink, 10% of them have a real possibility to develop alcoholic chronic pancreatitis in the near future. This can cause a huge problem for the American health care system by bringing in crowds of disabled people.

Approximately 5 to 6 years after the onset of the disease (especially in patients who continue to drink), patients with chronic pancreatitis seek medical attention for persistent pain. In most cases, only pain can bring individuals with alcohol abuse, particularly males, to the doctor. It is known that males, especially alcoholics, consider themselves healthy and only severe pain can change their opinion to visit the doctor. This is a crucial time for the alcohol depended individual to cease the progression of pancreatic damage. There are many difficult tasks that have to be performed simultaneously.

By common sense, effective action needs to be undertaken in the early reversible stages such as *acidic pancreas and bile* and *pancreatic deficiency* stages to postpone *pancreatic failure*. Later, in the Chapter 40. *Biotherapy Outpatient Program for Alcohol Cessation*, there is a rehabilitation program of alcoholic pancreatitis in the early stages.

Interesting facts at a glance:

In Western countries, alcohol is the most frequently associated factor of chronic pancreatitis, involved in 50% to 80% of cases

Clinically, alcoholic chronic pancreatitis is characterized by recurrent attacks of abdominal pain. That shows the continuation of pancreatic damage

A dose-response relationship was found between the average volume of alcohol consumption and pancreatitis. 40-50 g of pure alcohol per day can trigger chronic pancreatitis. For now, researchers disagree upon the root cause by which alcohol causes chronic pancreatitis

Only 10% of heavy alcoholics suffer from severe chronic pancreatitis

There are some unknown factors that predispose alcohol addicts to the development of pancreatitis

The combination of whole body acidity with direct toxic influences of alcohol and its acidic metabolites on the pancreatic cells are the key to understanding the prevalence of pancreatitis after alcohol consumption

Most alcohol abusers suffer from Sphincter of Oddi Dysfunction and dysbiosis (Candida-yeast overgrowth)

Individuals with Candida-yeast overgrowth constantly produce their own alcohol

The development of acute and chronic alcoholic pancreatitis is triggered by metabolic acidosis and consequent harmful changes in biochemistry of pancreatic juice and bile

Excess of proteins and fats in the diet can play a role in the onset of alcoholic pancreatitis

Smoking is focused on for its possible role in the development of alcoholic chronic pancreatitis as well

Alcoholic pancreatitis is a very complicated problem and needs a comprehensive rehabilitation program that focuses on early (reversible) stages of this disease

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Chapter 12-Biliary Pancreatitis

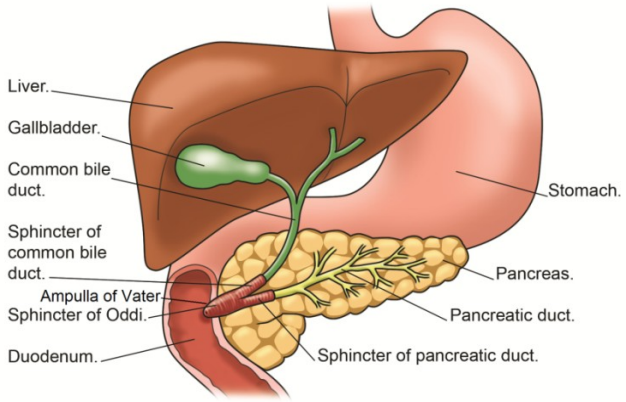
For individuals lacking a medical background

Beside alcoholic pancreatitis, there is another inflammation condition called billiary pancreatitis. **Biliary** refers to the association with the bile or the gallbladder.

The old European doctors knew that if an individual suffered from chronic pancreatitis, that they should also look for liver or gallbladder problems.

The health of the liver and gallbladder is inextricably bound to the health of the pancreas

To understand the liver/pancreas connection it is necessary to recognize that all of the organs of the upper GI tract (such as the stomach, liver, gallbladder, pancreas and duodenum) work together as a unit. If any single organ fails, then the whole system is thrown out of order. Digestive hormones and the nervous system are also vital to the proper functioning of these gastrointestinal organs. More information can be found in the Chapter 5. *Pancreas, liver, and bile: counterparts or huge enemies* in this book.



The liver, our chemical plant, performs many vital tasks. Everything we eat makes its way to the liver, and the liver uses food to produce vital nutrients for our cells - and for the whole body. Also importantly, the liver manufactures and releases bile. Bile facilitates the process of digestion and bile is also a vehicle for removing toxic garbage from body.

How does liver remove toxins from the body? There are two types of toxins: water-soluble substances and fat-soluble substances. The liver makes water-soluble waste less toxic and releases it into the bloodstream. The blood then moves the waste products to the kidneys for elimination from the body. Next, the liver breaks down the fat-soluble waste, makes it less toxic and then moves it into the bile. Bile pushes this waste through the small and large intestines and out of the body.

We can look at bile as a river for garbage and bile ducts as waste pipe lines. The process starts when liver cells secrete bile into a network of small ducts. These many small ducts meet to form the common bile duct, which carries bile from the gallbladder and liver.

The common bile duct then joins with the pancreatic duct. The pancreatic duct carries the pancreatic juice containing digestive enzymes from the pancreas into a small cavity, the Ampulla of Vater. A blend of bile and pancreatic juice goes through the Ampulla of Vater into the duodenum.

It is very important that the pressure in the pancreatic duct is always higher than the pressure in the bile duct so that bile cannot reach the pancreatic cells. Why is this important? Scientists proved that even the tiny amount of bile occurring in the pancreatic ducts can activate pancreatic digestive enzymes, thus causing dangerous inflammation of the pancreas that is referred to as **biliary pancreatitis**.

There are a few possibilities when the bile can reach the pancreatic duct.

The duodenum wall has a muscle valve called the Sphincter of Oddi. The Sphincter of Oddi controls secretions from the liver, pancreas, and gallbladder moving into the duodenum section of the small intestine.

Spasms or blockage of the Sphincter of Oddi may cause bile and pancreatic juice to back up, thereby increasing the pressure inside the pancreatic duct. Therefore, bile can go the "wrong way" into the pancreatic duct. Bile and digestive enzymes fastened up inside the pancreas, causing digestive enzymes to be activated. As a result, self-digestion begins of its own pancreatic cells. Self-digestion is a dangerous process that damages the pancreas leading to inflammation, pain, congestion and as a final point the deterioration of pancreatic tissue.

If the bile is thick, it is difficult for the bile to move smoothly throughout the ducts and Sphincter of Oddi. This happens during cases of hepatitis, fatty liver, parasites, congestion, or inflammation of the liver, infection and other liver and gallbladder problems.

In addition, gallbladder stones can block bile movement, increasing the pressure into the Ampulla of Vater and backing up the bile and pancreatic juices. This is a condition that doctors call biliary pancreatic reflux or “wrong way traffic” for bile. If this happens, aggressive bile burns and irritates the walls of the ducts and pancreatic tissue. When travelling the wrong direction to the pancreas, toxic aggressive bile with gallbladder stones destroys the pancreatic cells causing premature activation of digestive pancreatic enzymes inside the pancreas. Bile can cause the self-digestion inside the pancreas - biliary pancreatitis.

There are many causes of gallbladder stones, including poor eating habits, body acidity, hormonal changes, lack of exercise, age and being overweight or obese. If individuals start intensively losing weight, ether by "crash" diets or after gastric bypass surgery, gallbladder stones are formed. The size of gallbladder stones can range upwards from the size of a piece of sand. Even small gallbladder stones can cause spasms of the Sphincter of Oddi and promote biliary pancreatitis, as well.

A physical blockage of the Sphincter of Oddi can stop the smooth flow of pancreatic fluid and bile. Gallstones can cause the blockage of the Sphincter of Oddi, as well. The mix of pancreatic juice and bile then becomes backed up into and increases the pressure in the pancreatic duct. Activated by the bile, pancreatic digestive enzymes can start to digest their own pancreas causing severe inflammation, pain and even death of pancreatic tissue. Nevertheless, having gallbladder stones does not mean biliary pancreatitis will be prevalent. In many cases, slipping gallbladder stones can cause mild attacks of the Sphincter of Oddi Dysfunction or spasms.

Reading special medical books or textbooks doesn’t give doctors the exact answer for what is the main trigger of biliary pancreatitis. Some individuals can pass large gallbladder stones without inflammation of the pancreas or they can have spasms of the Sphincter of Oddi or bile reflux but

without serious biliary pancreatitis. In 30% of cases, doctors make the diagnosis as "idiopathic" pancreatitis. This means that pancreatitis has no known cause.

The authors believe that severe chronic whole body acidity can cause changes in biochemistry of bile and pancreatic juice, which predispose pancreatic cells to damage. This, in turn, triggers the biliary pancreatic damages - pancreatitis. Acidic pancreas and bile are the origins of most of the pancreatic disorders and controlling this process is the key to prevent and heal the pancreas and gallbladder problems.

For individuals with a medical background

Biliary pancreatitis is associated with abnormalities of bile, bile ducts or the gallbladder.

In "*The Textbook of Gastroenterology*" Yamada T *et al*. (1999) wrote that gallstone disease and alcohol are the most common causes of recurrent acute pancreatitis in western countries.[81] Approximately one-fourth of patients, with biliary pancreatitis drink alcohol regularly. It can be assumed that both these harmful factors can damage the pancreas in unison.

Today, there are many opinions and theories, which attempt to explain the role of bile in the development of pancreatitis but this only shows the lack of a consensus even between specialists.

a. Biomechanical and Biochemical Bile Problems

Both biomechanical and biochemical bile problems may cause biliary pancreatitis; these problems typically occur together

In 1856, Claude Bernard first produced experimental pancreatitis by the injection of bile and olive oil into the pancreatic ducts of animals.

A century ego, Eugene Opie first associated gallstones (cholelithiasis) with pancreatitis and theorized that the impact of a gallstone at the ampulla of Vater produced "a common channel and pancreatitis from the entrance of bile into the pancreatic duct."

However, in many cases, individuals pass the large stones from the gallbladder without symptoms of pancreatitis. Pancreatitis may develop as a consequence of an impacted stone in the papilla of Vater and/or spasms of the Sphincter of Oddi, which obstruct the main pancreatic duct. Clinical evidence shows this is a very rare event occurring in no more than 5% of cases. [14]

Gallstone disease may manifest itself by the presence of:

1. Big gallbladder stones, even more than 2 cm
2. Very tiny stones, which are less than 2 mm in diameter
3. Gallbladder sludge

4. Calcium carbonate, cholesterol monohydrate and calcium bilirubinate crystals in the bile

This can reflect different stages of developing gallbladder stones. It is not necessary to have large gallstones, which block the pathway of bile. Some researchers also consider that small stones or biliary sludge may cause acute idiopathic pancreatitis.[79] Bile sludge is found in approximately 30% of patients with pancreatitis.[27, 80] According to Italian doctor Pier Testoni from San Raffaele Hospital of Milan,[14] bile crystals are present intermittently in the duodenal bile in 36-67% of patients with recurrent pancreatitis and documented gallstone disease. Other authors also confirm the role of occult gallstone disease in pancreatitis.[29, 30]

P.A. Testoni *et al*. (2000) found that occult gallstone disease accounted for 55% of the cases with the so-called "idiopathic" recurrent pancreatitis.[31] Over a 10-year period, Dr. P. Testoni identified a gallstone disease in 72.3% of 173 patients with a history of recurrent pancreatitis. [14]

Another proposed mechanism of causation of billiary pancreatitis is connected with the Sphincter of Oddi dysfunction. [81]

Some research postulates that the passage of a gallstone through the Sphincter of Oddi opens the sphincter for a short period of time, thus allowing the reflux of duodenal juice containing activated digestive enzymes going into the pancreatic ductal system. Another idea is that spasms of the Sphincter of Oddi increase the pressure inside the pancreatic duct with the consequence of pancreatitis.

Dr. P. Testoni [14] considered that pancreatitis can develop because of “transient papillary oedema or papillary orifice relaxation following the recent passage of stones which can obstruct the pancreatic juice flow or promote duodenal-pancreatic reflux, respectively”.
However, the observation shows that procedures designed to make the sphincter incompetent, such as sphincterotomy, do not regularly cause pancreatitis.

It has been suggested that a simple mechanical explanation whereby increased pressure in the pancreatic duct causes rupture of the smaller ductules and leakage of pancreatic juice into the pancreatic tissue. Although the pancreatic duct fluid pH is maintained in the range of 8.0 to 9.0 by the secretion of bicarbonate, the interstitial pH of 7.0 within the pancreatic parenchyma favors activation of trypsin.

Many researchers believe that the direct destruction of acinar cells from elevated pancreatic duct pressure is a more likely a provoking event. Post – ERCP (Endoscopic Retrograde Cholangiopancreatography) pancreatitis is usually used as an example to support this idea.[332]

Numerous debates discuss the role of the bile reflux of the development of pancreatitis. Reflux of bile into the pancreas is a well-known risk factor for the development of biliary pancreatitis but this theory has some controversies and is difficult to prove experimentally.

In the last decade, thanks to the work of David C Whitcomb, MD, PhD and colloquies, pancreatic disease genes were indentified. Yet, Dr. D. Whitcomb wrote that "even in genetic predisposal people, development of biliary pancreatitis requires some additional environmental, metabolic and immune factors".[12]

The fact is that only small percentages of patients with gallstones suffer from pancreatitis. The mechanism by which a gallstone may cause pancreatitis is not entirely clear.

The passing of large gallstones does not suggest development of pancreatitis

Most researchers and doctors agree that the predisposition reason or trigger factors causing damage to the pancreas leading to the development of biliary pancreatitis can be unknown.

Existing gallbladder stones do not necessarily develop billiary pancreatitis. It is possible that the development of gallbladder stones and the predisposition for biliary pancreatitis have the same origin and the same biochemical pathogenic changes.

It is our belief, that because of the simultaneous changing of pancreatic juice and bile biochemistry due to chronic metabolic acidosis and deficiency of electrolytes and bicarbonate, that billiary pancreatitis can be developed.

b. Basis of Biliary Pancreatitis

It is the opinion of the authors, that there are two main interactive reasons for biliary pancreatitis:

1. Acidification of bile and changing of the biochemistry of bile, which cause bile to be "aggressive", corroding and irritating for the mucous walls of bile ducts, Sphincter of Oddi, pancreatic duct and duodenum. This leads to spasms and bile reflux to the pancreatic duct and activation of digestive pancreatic enzymes inside the pancreas. Bile acidity usually combines with acidic changes in the pancreatic cells and biochemistry of pancreatic juice. This, in its turn, also may promote trypsin activation inside the pancreas and consequent self-digestion and inflammation

2. Bile acidification and changing of the biochemistry of bile, especially the precipitation of the bile acids and calcium salts, and changing in cholesterol/phospholipids ratio. This can cause formation of gallbladder stones, sand and sludge, which induce irritation and spasms of the Sphincter of Oddi, or/and mechanical obstruction with increasing the pressure inside the pancreatic duct, bile reflux to the pancreatic duct, etc

Chronic metabolic acidosis – the body's acidity, harmfully influences both the pancreas and bile quality. More on this matter can be found in the Chapter 4. "*Acidity kills the Pancreas*" and Chapter 5. "*Pancreas, liver, and bile: counterparts or huge enemies*".

It is known that liver cells produce approximately one liter of the liver bile: a bitter, alkaline, brownish-yellow fluid that is stored in the gallbladder and discharged into the duodenum and aids in the emulsification, digestion, and absorption of fats. Bile also contains many poisonous substances because it is a vehicle for removing fat-soluble toxins, heavy metals, drugs, medication, and other chemicals from the body.

Liver bile flows into the common hepatic tract, which joins with the cystic duct from the gallbladder to form the common bile duct. The common bile duct, in turn, joins with the pancreatic duct to empty into the duodenum.

If the Sphincter of Oddi is closed, bile is prevented from draining into the duodenum and instead flows into the gallbladder, where it is stored and concentrated to up to five times its original potency between meals. This concentration occurs through the absorption of water and electrolytes, while retaining all the original organic molecules. In the case of chronic metabolic acidosis, the blood buffer system is depleted. To keep proper blood pH, more electrolytes and bicarbonate move out of the bile into the blood so that the pH of bile decreases to the acidic range.

The gallbladder can be another important organ to help the body keep the constant slightly alkaline terrain inside the blood. The gallbladder can even be self-sacrificed when the organism undergoes serious acidic conditions

Cholesterol is also released with the bile and is dissolved in the bile salts and lipids. 75% of the gallbladder stones are cholesterol stones. The remainders are pigment stones that precipitate with calcium.

S. Lambou-Gianoukos from the University of Massachusetts Medical School wrote in her work *Bile Metabolism and Cholelithiasis* (2008) [84] , that an acidic bile pH promotes the super saturation of bile with calcium cations (calcium carbonate) and that allows the precipitation of calcium salts, which promote manufacturing of gallbladder stones.

The liver bile contains about 97% water. After a few hours in the gallbladder, the percentage of water in the bile decreases to 85%. Acidification and concentration of the bile removes some of the gallbladder's constituents out of the solution, so they precipitate causing gallbladder stones.

c. Bile and Acidity

In what situations can acidifying the bile (lowering pH) promote gallbladder stone formation? One of the predisposal factors for developing gallbladder stones is chronic metabolic acidosis or whole body acidity.

Facts, which support this idea include:

> The liver and pancreas suffer the most from whole body acidity. Acidity of liver and gallbladder bile lead to the precipitation of bile acids. 50% of the bile acids were precipitated at pH less than 5, compared with only 26% at pH greater than 6. These findings of Fitzpatrick W J

et al. (1986) suggest that pH dependent bile acid precipitation can also limit lipid solubilisation. [75] If cholesterol becomes less soluble, it precipitates and promotes gallbladder stone manufacturing

> Individuals that consume a high consumption of acid forming food (sugar, meat, white flour, trans fatty acids, etc.) have a high level of body acidity as well as a high prevalence of gallstones

> Both the chronic metabolic acidosis and gallbladder stones prevail in particular individuals (diabetes, overweight issues and over the age of 60)

> Another connection between acidic conditions and gallstones is rapid weight loss. Fasting and dieting are risk factors for manufacturing and releasing gallbladder stones. About one-third of all patients having surgery for obesity develops gallstones. [83] Rapid weight loss frequently leads to serious changes in fat and carbohydrate metabolism. This process causes ketoacidosis, where very acidic ketons are collected in the blood

> In whole body acidity, the organism borrows minerals (especially calcium from bones) to neutralize acidification. During metabolic acidosis, calcium leaves bones (osteoporosis) and goes into the blood (atherosclerosis with calcification of arteries). Calcium also collects into the gallbladder mostly as calcium carbonate. Many scientists support the importance of calcium precipitation in the process of manufacturing gallbladder stones

> Chronic metabolic acidosis has a link to insulin resistance and consequently, the Metabolic Syndrome. This leads to high blood cholesterol and triglycerides in blood and bile. This changes the ratio between cholesterol and phospholipids and may cause precipitation of cholesterol crystals in the bile, thus manufacturing gallbladder stones

There are many other triggers of metabolic acidosis: alcohol, some medications, sedentary lifestyles, stress, fasting, hereditary or acquiring gene mutations, parasites, Candida –yeast overgrowth, dehydration, Metabolic Syndrome with high triglycerides, etc. Today, chronic metabolic acidosis occurs commonly, especially in the West and in westernized societies. Thus, gallstone diseases arise.

It has been estimated that in the United States approximately 20 million individuals harbor gallstones. Notably, gallbladder removal surgery (cholecystectomy) is the most common elective abdominal operation performed in the United States, with more than 700,000 operations performed annually.

It is believed that gallstone disease is a leading cause of 30-50% of acute biliary pancreatitis cases, more common in the elderly.

d. Gallstones and Exocrine Pancreatic Deficiency Disorders

Gallstone disease has a direct connection with exocrine pancreatic deficiency disorders

1. *Acidic pancreas and bile* associates with the functional stage of gallstone disease. There are so far no structural damages; as a result, there are minimal changes in the tests. Possible diseases and conditions associated with this stage are biliary dyskinesia, Sphincter of Oddi Dysfunction type III, functional dyspepsia, etc.

2. In *pancreatic deficiency* stage, some structural damages cause aggravation of symptoms of gallstone disease with possible pancreatic damage. Lab tests, imaging and endoscopic tests reveal gallbladder stones and injuries in the gallbladder, pancreas, bile and pancreatic ducts. Possible diseases and conditions associated with this stage are attacks of acute biliary pancreatitis (some of them maybe very mild), chronic pancreatitis, Sphincter of Oddi Dysfunction type I or II, gallbladder disorders (inflammation, stones, sludge, parasites), conditions after gallbladder removal, etc.

Almost everyone with acute biliary pancreatitis suffers severe abdominal pain in the right upper abdomen or below the breastbone (sternum). The pain in acute pancreatitis, which is caused by gallstones, often penetrates to the back in about 50% of cases. The pain usually starts suddenly and reaches its maximum intensity in minutes. The pain then remains steady and severe and brings people into the ER. Nausea, vomiting, chills, jaundice and skin itching may accompany these attacks. Sometimes stool may be pale or clay-colored.

3. Symptoms of biliary chronic pancreatitis in the *pancreatic failure* stage include constant abdominal pain, indigestion, steatorrhea (smelly stools containing oil) and weight loss. Other symptoms of biliary chronic pancreatitis are fever, chills, jaundice, sweating and weakness. Diagnosing chronic biliary pancreatitis in this stage can more or less be easy to verify by conventional tests. Possible diseases and conditions associated with *pancreatic failure* are the final stage of chronic biliary pancreatitis, liver cirrhosis, and cancer.

Part III. HOW TO IMPROVE THE EXOCRINE PANCREATIC FUNCTION, POSTPONE PANCREATIC DETERIORATION, AND HEAL PANCREATIC DISEASE will focus on the nondrug and non-surgery approaches for healing common billiary disorders and pancreatitis. Pragmatically, it is vital to pay more attention on *acidic pancreas and bile* and *pancreatic deficiency* stages of exocrine pancreatic deficiency to avoid nonreversible damages of the pancreas leading to billiary pancreatitis.

Interesting facts at a glance:

The health of the liver and gallbladder is inextricably bound with the health of the pancreas

If “aggressive” bile occurs in the pancreatic ducts it can activate pancreatic digestive enzymes, therefore causing dangerous inflammation of the pancreas called biliary pancreatitis

Bile biomechanical and biochemical problems cause biliary pancreatitis; they typically occur together

Sphincter of Oddi Dysfunction, biliary refluxes and gallbladder stones implicate the possible development of biliary pancreatitis

Acidification of the bile leads to severe biochemical abnormalities

These biochemical abnormalities make bile 'aggressive" with irritation of surrounding tissues and consequent spasms, erosions, ulcers, and activation of the proteolytic enzymes inside the pancreas causing self-digestion and biliary pancreatitis

Bile acidification and changing of the biochemistry of bile, especially the precipitation of the bile acids and calcium salts and changing in cholesterol/phospholipids ratio that "can cause formation of gallbladder stones"

Pragmatically, it is vital to focus on acidic pancreas and bile and pancreatic deficiency stages of exocrine pancreatic deficiency to prevent non-reversible damages of the pancreas leading to billiary pancreatitis

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Chapter 13-Chronic Pancreatitis =>Pancreatic Cancer

For individuals lacking a medical background

After the death of Steve Jobs, "Pancreatic cancer" sounds even scarier. Pancreatic cancer is the fifth leading cause of cancer death in the United States as well as around the world. According to the American Cancer Society, about 38,000 individuals are diagnosed with pancreatic malignancy and roughly 34,000 individuals die from this disease every year. Roughly, 5 percent of people diagnosed with this type of cancer will survive five years from the diagnosis, according to the American Cancer Society. Even after surgery, however, this cancer has a high recurrence rate.

According to http://www.Mayoclinic.com, pancreatic cancer is seldom detected in its early stages. Difficulty with early diagnosis is one of the reasons why pancreatic cancer is a leading cause of cancer death. Symptoms of the disease may not appear until the cancer has progressed. At that point, the cancer has likely spread to other organs in the body, which may make surgery impossible. The cancer surgeon usually removes part of or the whole organ that is involved in the cancer growth. The pancreas is a small gland with many vital tasks, hence taking out the pancreas creates a lot of problems to sustain life.

What comes to mind, particularly to those with chronic pancreatitis, when they hear or think about pancreatic cancer? "Thanks God, it is not me" or "What should I do to avoid that?"

Simple common measures to keeping the pancreas healthy include:

- Decreasing the amount of inner toxicity by using different cleansing techniques, food supplements and keeping a healthy diet and lifestyle

- Promoting the normal function of bile and pancreatic ducts by using proper food combinations and herbs, drinking healing mineral water made from the Genuine Karlovy Vary Thermal Spring Salt and undertaking relaxation techniques, chiropractor manipulations and regular acupuncture

- Decreasing the amount of yeast and fungus in the body by an anti-Candida diet, restoring of the friendly intestinal flora and undergoing colon hydrotherapy

- Keeping the internal milieu slightly alkaline by proper dieting, mineral supplementation and drinking healing mineral water made from the Genuine Karlovy Vary Thermal Spring Salt

- Stopping smoking and the consumption of alcohol

These measures are important for healthy people and individuals with pancreatic, liver, and gallbladder problems. Individuals with chronic pancreatitis are at a higher risk of developing pancreatic cancer, especially if they continue smoking and consuming alcohol.

From an advertisement "*in 2010, 200,000 individuals stopped smoking forever. This was due to the fact they had died from cancer*".

Improving the health of the pancreas may help to prevent the development of pancreatic cancer. Nowadays pancreatic cancer statistics are not so optimistic and treatment of this life threatening disease is very limited. Cancer strikes mostly weak and sick organs, so this book is dedicated to keep the pancreas healthy as much as possible.

For individuals with medical backgrounds

Anatomy

In up to 90% of cases, pancreatic cancer arises from the cells, which line the pancreatic ducts. About three-quarters of pancreatic tumors arise in the head and neck of the pancreas - the anatomic parts through which the pancreatic duct runs just before it meets the duodenum. At this location, the liver bile mixes together with pancreatic juices in a small space – the hepatopancreatic ampulla also called the "Ampulla of Vater."

It is known that even just a small amount of bile in the pancreatic duct causes activation of digestive enzymes inside the pancreas, which leads to self digestion of tissue and inflammation – pancreatitis. The blended secretion of bile and pancreatic juice goes through the opening to the duodenum. The opening has a muscular valve called the Sphincter of Oddi that controls secretions from the liver, pancreas, and gallbladder into the duodenum of the small intestine.

Spasms or blockage of this valve may cause back up of the pancreatic juice and increase the pressure inside the pancreatic duct. Entrapped inside, the pancreatic digestive enzymes start to digest their own pancreas causing congestion and inflammation. It is known that the persistent inflammation and congestion may also cause cells' mutation and cancer.

Some risk factors along with stress cause the spasms of the valve. Constant exposure of toxic substances from the bile into the pancreas is the major factor in the development of pancreatic cancer.

a. Who is at Risk for Pancreatic Cancer?

The lifetime risk odds of having pancreatic cancer are about 1 in 76. The risks may be changed by certain risk factors including:

> Age: A large amount of these cancers occur in people over the age of 60. 70% are older than age 65

> Smoking: Cigarette smokers are two to three times more likely than nonsmokers to develop pancreatic cancer. Howes *et al*. [34] also found a median age of cancer onset in the EUROPAC study of 71 years of age in nonsmokers and 56 years of age in tobacco smokers. These studies provide striking examples of the mixture effects of risk factors that together contribute to the development of the disease

> Health Conditions: Pancreatic cancer occurs more often in individuals who have diabetes, hepatitis, liver cirrhosis, surgery to the upper digestive tract and, evidently, chronic pancreatitis. There is a significant increase in the risk of pancreatic cancer among patients with chronic pancreatitis, noted by Lowenfels *et al.* (1993) [35]

> Diet: There is a link between pancreatic cancer and a high sugar/high saturated fat diet that includes a lot of red meat, pork, and processed meat (such as sausage and bacon). On the other hand, some studies have found that diets high in fruits and vegetables may help reduce the risk of pancreatic tumors

> Work Exposure: Heavy exposure at work or home to certain factors (toxic chemicals, pesticides, dyes, solvents, gasoline chemicals and ionizing radiation) may increase the risk of getting pancreatic cancer

> Family History: Pancreatic cancer seems to run in some families. A family history of colon or ovarian cancer increases the risk of pancreatic cancer

> Alcohol: About 7 out of 10 cases of chronic pancreatitis are due to long term heavy drinking. Chronic pancreatitis is a known a high risk factor for the pancreatic tumor

> Being **overweight** or **obese** raises a person's risk of pancreatic malignancy. This is especially true for individuals with belly fat. This is a symptom of insulin resistance or metabolic syndrome and this disease raises the risk of several types of cancer including breast and colon, as well as diabetes, high blood pressure, heart disease and other conditions. Overweight people are more likely to develop this cancer, as are those who don't get much exercise

b. Chronic Pancreatitis Connection

Pancreatic adenocarcinoma remains one of the worst of all cancers. It is difficult to predict, detect, and diagnose. It is resistant to all current treatments except early surgery. Recent interest has focused on possible genetic links. Indeed, a number of familial syndromes are associated with pancreatic cancer, but only a minority of patients with pancreatic cancer has a strong family history of pancreatic cancer. If genetic heredity is not a marker for pancreatic cancer, then the "heredity of lifestyle" is. The way an individual eats, lives, works, spends free time, uses drugs and alcohol, etc., may predict the potential catastrophe.

The one consistent risk factor for pancreatic cancer is chronic pancreatitis.

The process leading to chronic pancreatitis appears to require the interaction of environmental factors; factors that lead to recurrent pancreatic injury, and/or an altered immune response leading to chronic inflammation and fibrosis. All of these mutations point to defects in the mechanisms protecting the pancreas from premature trypsinogen activation, which causes injury by activating other digestive enzymes, which, in turn, leads to pancreatic auto digestion and an inflammatory response.

The environmental factors associated with chronic pancreatitis (e.g., alcohol, tobacco smoking) appear to facilitate chronic pancreatitis by lowering the threshold for initiating trypsinogen activation within the acinar cells, impairing pancreatic duct cell secretion, or modulating the immune system to favor chronic inflammations or fibrosis. Inflammation alone usually does not lead to cancer. However, once chronic pancreatitis is initiated, it appears to progress unrelentingly toward inflammatory destruction of the total organ and provides a milieu for the development of pancreatic cancer. The risk of pancreatic cancer markedly increases after the age of 50 years, which is about 30 years after the onset of chronic pancreatitis.

In 2004, David C. Whitcomb in his article " *Inflammation and Cancer V. Chronic pancreatitis and pancreatic cancer*" wrote that one consistent risk factor for pancreatic cancer is chronic pancreatitis.[33] This observation has now been supported through multiple epidemiology studies in chronic pancreatitis, which all show an increased risk for pancreatic cancer. Professor D.C. Whitcomb also emphasized that "gene mutations are not directly important in the development of pancreatic cancer, but rather lead to a high-risk inflammatory milieu".

Chronic pancreatitis occurs with recurrent injury to the pancreas when the normal healing process fails and chronic inflammation develops. Pancreatic cancer develops in subjects with chronic pancreatitis after failure of multiple protective mechanisms. Smoking likely exaggerates this process. "In summary, chronic pancreatitis, independent of the underlying cause, over the course of a number of decades, markedly increases the risk for pancreatic carcinoma".[33]

c. Acidity Plays the Crucial Role in Pancreatic Cancer

The pancreas is the "alkaline" gland, which, similar to the liver, mostly suffers from chronic acidosis condition. Acidity plays the crucial role in the development of pancreatic cancer, as well. Needless to say, individuals with any cancers are usually very acidic.

The simple way to verify chronic metabolic acidosis at home is measuring saliva and urine pH in the morning and evening by litmus paper for one week. Acidic saliva and urine - pH less than 6.6 shows the organism is overloaded with acidic radicals and tries to eliminate them through the body fluids.

Cancer patients typically have saliva and urine pH less than 6.6 (very acidic)

Chronic pancreatitis patients have an increased risk of developing pancreatic cancer. The cause of this increase has yet to be fully explained, but smoking and inflammation may play an important role. Patients with chronic pancreatitis very often present pancreatic exocrine insufficiency combined with a persistently low duodenal pH in the postprandial period. [36] This shows the acidic metabolic state and the decreasing of alkaline pancreatic juice production because of the low amount of minerals and bicarbonates in it.

There is evidence that bile reflux may cause cancer in the pancreas and stomach, as well.[37]

The idea about the link between acidity and cancer is not new one. In 1956, Dr. Otto Warburg, two time Nobel Prize winner, stated in his work, "*On the Origin of Cancer Cells*" that healthy cells thrive in an environment of oxygen while cancer cells thrive without oxygen by a fermentation of sugar in an acidic environment. Oxygenation and pH of the blood are interrelated. Normal pH of the blood means that the blood is capable of carrying more oxygen. On the other hand, low pH (acidic) leads to a decreased amount of oxygen in the blood, thus less oxygen goes into the cells.[315]

“The era in which fermentation of the cancer cells or its importance could be disputed is over, and no one today can doubt that we understand the origin of cancer cells if we know how their large fermentation originates or, to express it more fully, if we know how the damaged respiration and the excessive fermentation of the cancer cells originate”.

Otto Warburg. *On the Origin of Cancer Cells* http://www.sciencemag.org/content/123/3191/309

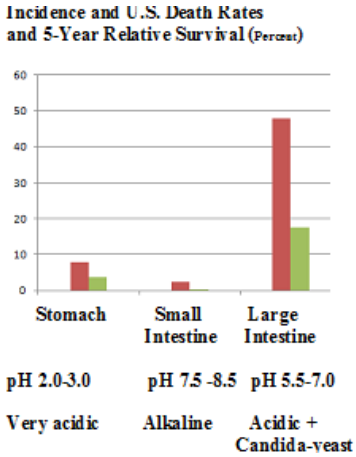
Cancer cells require low oxygen and an acidic environment to survive and flourish. From the authors’ experience, most people with advanced cancer have saliva and urine pH less than 6.4. This means that there is severe acidity and low amounts of oxygen at the cellular level.

d. Possible Role of the Dysbiosis (Candida-Yeast Overgrowth, SIBO) in Pancreatic Cancer

Some researchers and doctors suppose that both metabolic acidosis and dysbiosis may be two primary reasons for cancer cell overgrowth.

There is data from the National Cancer Institute Cancer Statistics Review 1975-2007 about incidence of the cancer in US. http://www.seer.cancer.gov/statfacts/html/

To our knowledge, Incidence Rate = (New Cancers / Population) × 100,000



In the picture above, there are levels of evidence of the cancers and pH of the stomach, small intestine, and large intestine.

Statistics show that cancer of the small intestine in the normal condition is a very rare disease. Why? Probably because the small intestine is the most alkaline place in the gastrointestinal tract. Contrary, the large intestine is acidic, where Candida-yeast overgrowth is more prominent. Colon cancer is the third most common cancer type, and the second leading cause of cancer death in the U.S.

http://www.cancer.org/Cancer/ColonandRectumCancer/DetailedGuide/colorectal-cancer-key-statistics

Researchers have studied pH in different areas of the GI tract by having patients swallow the Heidelberg pH capsule that continuously transmits the pH level to the medallion transceiver (worn by the patient). Therefore, it is found that the stomach and colon have pH less than 7.0 (acidic) and the small intestine pH is more than 7.0 (alkaline).

Tullio Simoncini, an Italian doctor-oncologist, propones the Fungal Hypothesis of Cancer. Dr. Simoncini considers that a fungal infection is the source of cancer cell creations. The growth of the fungal colonies, especially *Candida albicans*, together with the reaction of the normal cells, which try to protect themselves against the fungal infection, causes the tumors. As a method of treatment, Dr. Simoncini delivered alkaline solutions directly into the cancer tumor with positive results. http://www.cancerisafungus.com/about-dr-simoncini.php

Putting in account the pandemic of the metabolic acidosis, dysbiosis (Candida-yeast overgrowth) and digestive (pancreatic) disorders may give the answer why pancreatic cancer is on the rise.

e. Alcohol Connection

Consuming two or more drinks per day could increase the risk of pancreatic cancer by about 22 percent, according to new data published in the *Journal of the American Association for Cancer Research*. This is one of the largest studies to look at the dietary factors in relation to pancreatic cancer risk. [38] A drink is defined as 12 ounces of beer, four ounces of wine, or 1.5 ounces of 80-proof distilled liquor.

It is easier to prevent pancreatic cancer rather than treating it, especially in predisposed individuals. Those who have chronic pancreatitis are at a higher risk of developing cancer. Improving the health of the pancreas may help to prevent developing pancreatic malignancy.

What may help to improve the pancreatic health to lower the risk of pancreatic cancer?

> **Acupuncture** can normalize the function of the liver, gallbladder, pancreas and open the bile duct, pancreatic passages and valves. Acupuncture improves microcirculation and immunity and decreases pain and stress

> European individuals with pancreatic problems have used **Healing Mineral Water Prepared from the Karlovy Vary Thermal Spring Salt** for hundreds of years. Drinking this mineral water decreases congestion and pancreatic juice back up, promotes the proper acid-alkaline balance, improves digestion and normalizes activity of digestive enzymes

> Herbal Medicine has a long history of being used by individuals with pancreatic problems

> Hypnosis and **Acupuncture** can help to avoid smoking and stop drinking alcohol

> Nutritional Supplements can help to decrease oxidative stress, inflammation, pain, promote digestion, and normalize acid-alkaline balance

> A proper organic alkaline **Pancreatic Diet** can decrease acidity and diminish inner toxicity and irritation of the pancreas

> Regular **Exercises, Chiropractic Manipulations** and **Point Massage** can improve regulation and function of the pancreas

> Restoration of Friendly Intestinal Flora by using **Colon Hydrotherapy** and **Probiotics** can help with digestion, improving immunity, diminishing yeast in the body and promote overall well-being

> Whole Body Cleansing decreases the inner toxicity and improves the natural body's detoxification

The chain reaction: **Acute Pancreatitis => Chronic Pancreatitis => Pancreatic Cancer** can be really slowed by changing the lifestyle and using alternative medicine.

If one is already diagnosed with pancreatic cancer, then there are two possibilities:

First, the patient shall undergo surgery, chemo and/or radiation therapy. During that time, taking some supplements may interfere with the above therapies. However, even in this situation, a healing diet, restoration of friendly intestinal flora, drinking healing mineral water prepared from

genuine Karlovy Vary spring salt and acupuncture may alleviate the side effects of surgery, chemo, and/or radiation therapy.

Second, for various reasons, the patient elects not to have surgery, chemo, and/or radiation therapy. Alternative therapies that are described in this book may improve the quality of life and possibly prolong the lifespan.

Interesting facts at a glance:

Pancreatic cancer is one of the worst cancers

Pancreatic cancer has grown in Western countries the past few decades, which shows that environmental factors, such as diet, lifestyle, external and inner toxicity, dysbiosis, metabolic acidosis, etc., may implicate this process

Chronic pancreatitis, independent of the underlying cause, over the course of a number of decades, markedly increases the risk for pancreatic cancer

All measures to prevent pancreatitis and keeping the pancreas healthy are also important in decreasing the risk for pancreatic cancer

Decreasing the amount of inner toxicity by using different cleansing techniques, food supplements and a healthy diet and lifestyle will aid in keeping the pancreas healthy

Promoting the normal function of bile and pancreatic ducts by using proper food combinations, herbs, drinking healing mineral water made from the Genuine Karlovy Vary Thermal Spring Salt, relaxation techniques, chiropractor manipulations, and regular acupuncture shall also aid in pancreatic health

Decreasing the amount of yeast and fungus in the body by an anti-Candida diet, herbs, food supplements, restoration of the friendly intestinal flora and colon hydrotherapy may improve pancreatic health

Keeping the internal milieu slightly alkaline by proper diet, mineral supplements and drinking healing mineral water made from the Genuine Karlovy Vary Thermal Spring Salt shall keep the pancreas healthy

The chain reaction: Acute Pancreatitis => Chronic Pancreatitis => Pancreatic Cancer can be really slowed by changing the lifestyle and using alternative medicine

These measures may alleviate the side effects of surgery, chemo and/or radiation therapy

By themselves, these measures may improve the quality of life and possibly prolong the lifespan

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THE ROLE OF EXOCRINE PANCREATIC DEFICIENCY IN OTHER GASTROINTESTINAL DISORDERS

Chapter14-Functional Dyspepsia and Irritable Bowel Syndrome (IBS)

For individuals lacking a medical background

More than half of Americans have digestion problems. Millions complain of occasional or persistent gas, cramps, abdominal distension/bloating, nausea, fullness after eating, constipation, loose stool, or alternating of those conditions. They go to hospitals and undergo many examinations. Many of them receive the answer "There is nothing wrong with you", "Everything is in your head", "It is connected to stress", "Try to live with it", and so on. Many sufferers take medications or psych drugs and in the worse scenarios, undergo useless surgeries and procedures.

What Is Going On Here?

No question, our digestion vitally depends on the good quality of bile and proper function of the pancreas, its ability to produce the good amount of well working digestive pancreatic enzymes and a proper environment for these enzymes to do the right job.

Disorders of the bile and pancreas and the consequence of them – indigestion, in many cases, start slowly and can appear and disappear. It is very difficult to detect these disorders by simple tests or procedures in their beginning stage. They are called functional disorders. This occurs when the structure of the organs or systems does not change, but function improperly and the work is altered in the wrong direction.

Doctors use the word “functional” to describe symptoms or problems when they can find no anatomical abnormalities. The problem has to do with the function of the affected organs, where things don’t work or feel quite right. Symptoms of functional gastrointestinal disorders can occur anywhere in the gastrointestinal system.

Functional gastrointestinal diseases cannot be confirmed by simple, everyday tests and cannot be seen with the naked eye or even with endoscope or the microscope.

The most often Functional Gastrointestinal Diseases areDyspepsia and Irritable Bowel Syndrome (IBS) [123]

a. Dyspepsia

Dyspepsia is a derived Latin and Greek word meaning “difficult to digest”. Dyspepsia is commonly known as *upset stomach* or *indigestion*, meaning hard or difficult digestion. It is a medical condition characterized by chronic or recurrent cramps or mild pains in the upper abdomen, upper abdominal fullness and feeling full earlier than expected when eating. It can be accompanied by bloating, belching, nausea or heartburn. Dyspepsia is a common problem. Almost 35% of the world population suffers from functional gastrointestinal disorders, involving about 40% of gastroenterologist and 12% of primary care practices.[123]

Dyspepsia (indigestion) is a functional disease where the digestive organs, mostly the stomach and the first part of the small intestine, work abnormally. It is typically the chronic disease, in which the symptoms change in frequency and intensity.

Undigested food is collected in the gastrointestinal tube, where it ferments or rots. The body wants to eliminate this junk by using two open ends of the tube such as mouth and anus causing either vomiting or diarrhea.

Improperly digested foods lead to nausea, vomiting, belching, low appetite, and abdominal cramps. These symptoms can be considered as protective measures whereby the body prevents the entry of undigested food and toxins into the body. These measures also decrease the passage of chyme throughout diseased parts of the digestive tract, thereby minimizing possible pain. The symptoms of dyspepsia most often are provoked by eating, which is a time when many different gastrointestinal functions are called upon to work in concert. Dyspepsia tends to occur after meals, which gives rise to the notion that dyspepsia might be caused by an abnormality in the digestion of food.[39]

What Are The Symptoms of Dyspepsia (Indigestion)?

> Upper abdominal cramps or mild pain (above the navel)

> Belching

> Low appetite

> Nausea (with or without vomiting)

> Abdominal bloating (the sensation of abdominal fullness without objective distention)

> Early satiety (the sensation of fullness after a very small amount of food)

> Abdominal distention (swelling as opposed to bloating), gas

Eating often provokes these symptoms.

b. Irritable Bowel Syndrome (IBS)

While dyspepsia is a major functional disease in the upper part of the stomach, it is important to mention other functional diseases. A second major functional disease is Irritable Bowel Syndrome, or IBS. Irritable Bowel Syndrome (IBS) is the number one digestive disease in

America with 30-50 million sufferers. Some 22 % of the United States population has Irritable Bowel Syndrome (IBS) symptoms, either occasionally or persistently.

These disorders can have an upsetting impact on the quality of life of affected people. It is the second most common reason for absence from work or school (common colds are the main reason). Moreover, these disorders are very costly, drawing valuable resources from the care of more serious diseases. Acceptable treatment of functional digestive disorders has only limited effectiveness.

The symptoms of IBS are thought to originate primarily from the small intestine and/or colon and can occur together and change over the time. The key signs or symptoms of IBS are cramps, pain or discomfort in the abdomen. The other symptoms of IBS relate to the bowel habits such as

- Alternating between diarrhea and constipation
- Feelings of urgency (the need to find a restroom fast)
- Feeling of "incomplete" bowel emptying and more
- Loss of bowel control or soiling

Often, there can be a change in frequency or consistency of stool, primarily constipation or diarrhea. The symptoms can come and go and occur over a long period of time.

About 25% to 50% of individuals with IBS commonly report upper gastrointestinal (GI) symptoms as well such as:

- Intermittent upper abdominal discomfort or pain (dyspepsia)
- Heartburn
- Nausea
- Abdominal fullness
- Bloating, gas
- Early feeling of fullness (satiety)

Non-GI symptoms also occur. Sometimes, but not always, this may be due to an overlap of IBS with another condition. These symptoms include:

> Fatigue
> Muscle pain
> Sleep disturbances
> Depression and anxiety
> Sexual dysfunction
> Low back pain
> Headache

> Dizziness

In women, gut function appears to be influenced by changes in the levels of female hormones. IBS symptoms can become worse at certain times of the menstrual cycle.

In fact, dyspepsia and IBS may be overlapping diseases since up to half of patients with IBS also have symptoms of dyspepsia

Medical literature states that the causes of functional dyspepsia and IBS are unknown, and consequently, the cures of those chronic recurrent conditions are not likely. There is no specific treatment.

Pancreas and Functional Digestive Diseases

Many scientists found the connection between the lower function of the pancreas and development of functional digestive diseases. Without the proper amount and good quality pancreatic digestive enzymes, normal digestion is impossible.

The importance of effective pancreatic functions for overall health and proper gastrointestinal function in particular is rarely emphasized in the United States. The reason for this is the lack of laboratory evidence and specific physical symptoms to reveal the pancreatic disorders in the beginning stages. There is no the specific treatment of functional pancreatic disorders.

The authors consider that functional digestive disorders (when the patient has the symptoms, but doctors cannot find any abnormality in the tests), are the first functional stage of exocrine pancreatic deficiency disorder that we refer to as *acidic pancreas and bile*.

How Does the *Acidic Pancreas and Bile* Play A Role in Dyspepsia and Irritable Bowel Syndrome (IBS)?

A good quality and sufficient amount of pancreatic juice and bile are crucial for digestion of food and proper functioning of the whole gastrointestinal tract. Pancreatic digestive enzymes are essential to the body's absorption and full use of food.

The authors speculate that the main triggers of the development of functional digestive disorders are improper functioning of the pancreas and low quality of bile. Insufficient amounts of digestive enzymes and their low activity can disrupt normal digestion causing nonspecific symptoms of indigestion such as abdominal cramps, pain, bloating, heartburn, nausea, loose stool or constipation, fatigue, headaches, etc.

This, in turn, generates many chain reactions involving not only the GI tract, but also the whole body. For example, these chain reactions may include Candida-yeast overgrowth, food allergies or sensitivities, intestinal fermentation, putrefaction and the phenomenon known as high intestinal permeability, or "leaky gut syndrome", alternating constipation and diarrhea, undigested food and mucus in the stool.

Digestive pancreatic enzymes work as cleansing "janitors" for the gastrointestinal tract by digesting harmful microorganisms in the gut. Low activity of pancreatic digestive enzymes leads to an overgrowth of "bad guys" such as Candida-yeast, parasites and harmful bacteria in the small intestine.

On one hand, indigestion leads to a deficiency of essential nutrients, and on the other hand, produces toxic harmful substances. This influences the work of the nervous, hormonal and immune systems and causes chaos for the entire body. The problems caused by improper digestion are countless.

Acidification

It is the opinion of the authors that the corner stone of the lower function of pancreas is whole body acidity. More information can be found in the Chapter 4. "*Acidity kills the Pancreas*."
Due to whole body acidity, there is harmful acidic changing in the liver and bile.
Acidic bile becomes "aggressive" and causes irritation, spasms of the Sphincter of Oddi, bile refluxes and so on. The bile becomes thick, sticky, and full of the sludge and sand, which it is difficult to eliminate. Thickened bile cannot flow well.

The spasmodic Sphincter of Oddi also detains the bile inside the gallbladder. A low amount of bile increases toxicity because through the bile, the body eliminates fat-soluble toxic substances, chemicals, heavy metals, cholesterol, etc.

Furthermore, a low amount and poor quality of bile leads to constipation. An abundant flow of bile is essential to stimulate peristalsis. Peristalsis is the involuntary muscular movements of the small and large intestinal walls that move food along. Without sufficient stimulation by the bile the intestines become sluggish, resulting in constipation.

Any interference with healthy bile flow can create a myriad of immediate digestive symptoms, such as bloating, nausea, belching, fullness, heartburn, discomfort following meals and intolerance of fat.

Later, *acidic pancreas and bile* can cause problems in the lower abdomen such as diarrhea and flatulence. Acidity in the bile can cause precipitation of the bile acids and irritation of the bowel,

thus causing unexpected diarrhea. Acidification of the bile and inhibition of the normal bile flow suppress the digestion and absorption of fat. Besides the deficiency of vital fat-soluble substances and fat-soluble vitamins, a large amount of undigested fat causes fat malabsorption and diarrhea.

As can be seen, all symptoms of common functional digestive disorders such as functional dyspepsia and IBS may be explained by the decreased activity of pancreas and bile, which is the obvious problem of these conditions. Hence it follows; the treatment of functional digestive disease should focus on pancreas and bile health. Moreover, the earlier it happens, the more optimum results may be achieved.

For individuals with a medical background

Functional gastrointestinal diseases are those that involve abnormal functions of gastrointestinal organs in which the abnormalities cannot be verified by simple, everyday testing, and cannot be seen with the naked eye or even with the microscope or endoscope.

Often, the functional disorders of the gastrointestinal tract are categorized by involvement of the hollow digestive organ. Thus, in medical literature there are many names of functional gastrointestinal disorders of the esophagus, stomach, small intestine, colon, and gallbladder, such as the upset stomach, indigestion, nervous stomach, non-ulcer dyspepsia, irritable stomach, gastralgia, functional dyspepsia, neurogenic vomiting, neurosis of stomach, reflux, acid reflux, GERD, dysmotility of the small intestine, biliary dyskinesia, biliary colic, type III Sphincter of Oddi dysfunction, alcohol related dyspepsia, food sensitivity, visceral hyperalgesia, spastic colon, nervous colon, motility disorders of the colon, irritable bowel syndrome, post infectious irritable bowel syndrome, spastic colitis, constipation and so on.

Functional disorders of the pancreas are terra incognita in conventional medicine; there is little attention on the functional stage of exocrine pancreatic deficiency despite the pancreas being a key organ in normal digestion

In medical practice, it is common to use the medical term – dyspepsia.

The word "dyspepsia" was contrived by binding the Latin word "*dys*" (meaning “bad”) to the Greek word "*pepsis*" (meaning digestion), thus forming “dysdigestion” = indigestion.

Dyspepsia, or the abnormal digestion of food is one of the most common illnesses, affecting an estimated 20% of individuals in the United States.[119] Possibly only 10% of those affected actually seek medical attention for their dyspepsia.[39]

c. Prevalence of the Functional Dyspepsia

Below, there is prevalence of functional diseases in US. These statistics do not reflect the real picture. These official medical statistics do not include the large amount of individuals that did not seek conventional medical care such as those that came to alternative medicine practitioners, those without medical insurances, or those that considered their symptoms "as normal."

Functional Digestive Diseases in the U.S.[40]

Accepted from: Digestive Diseases Statistics in US. NIH Publication No. 06–3873 December 2005.
http://digestive.niddk.nih.gov/statistics/statistics.htm

First numbers are prevalence: the number of people in the United States affected by a disease or diseases in a year
Second numbers are hospitalizations per year
Third numbers are ambulatory visits per year

***Constipation*: 3.1 million people** (1996), **398,000** (2002), **1.4 million** (1999–2000)

***Non-ulcer Dyspepsia*: 6.4 million** new cases (1996), **79,000** (2002), **800,000** (1980s)

***GERD*: 20 % of the U.S. population** (1990), **710,000** (2002), **709,000** (1990–1992)

***IBS*: 22 % of the U.S. population, 119,000** (2002), **1.3 million** per year (1999–2000)

In their study "*Epidemiology of functional dyspepsia: A global perspective*" published in the *World Journal of Gastroenterology* in 2006, Mahadeva S, Goh KL stated that population-based studies on true functional dyspepsia (FD) are few, due to the logistic difficulties of excluding structural disease in large numbers of people. "Globally, the prevalence of uninvestigated dyspepsia (UD) varies between 7% - 45%, depending on the definition used and geographical location, whilst the prevalence of FD has been noted to vary between 11% - 29.2%. Risk factors for FD have been shown to include females and underlying psychological disturbances, whilst environmental/ lifestyle habits such as poor socio-economic status, smoking, increased caffeine intake, and ingestion of non-steroidal anti-inflammatory drugs appear to be more relevant to UD. It is clear that dyspepsia and FD in particular are common conditions globally, affecting most populations, regardless of location"[119]

d. Functional Dyspepsia and Irritable Bowel Syndrome (IBS)

While dyspepsia is a major functional disease, it is important to mention other functional diseases. A second major functional disease is the Irritable Bowel Syndrome, or IBS.

The symptoms of IBS include abdominal cramps or pains that are accompanied by alterations in bowel movements, constipation, or diarrhea. In fact, dyspepsia and IBS may be overlapping diseases since up to half of the patients with IBS also have symptoms of dyspepsia.

A third distinct functional disorder is non-cardiac chest pain. This pain may mimic heart pain, but it is not connected with heart disease. In fact, non-cardiac chest pain is thought to result from a functional abnormality of the esophagus.[39]

There is overlap between functional dyspepsia and irritable bowel syndrome when lower abdominal symptoms may also be present.[120, 125]

To examine the prevalence of gastrointestinal symptoms, Tutega AK and colleagues (2003) found a striking overlap between IBS and functional dyspepsia: 70% of individuals with IBS also had functional dyspepsia, whereas 43% of subjects with dyspepsia also had IBS. Moreover, more individuals with such overlap reported consulting a physician than those who had IBS or dyspepsia alone.[126]

Nicholas J Talley, MD, PhD, Professor of Medicine, Mayo Medical College of Medicine, Rochester, Minnesota wrote, "It is important to note that there was no predominant pattern of overlap identified consistent with a common underlying pathophysiology. Hence, artificial subdivision of these functional gastrointestinal complaints may not be particularly helpful in terms of management."[125]

According to Jay W. Marks, MD, a medical authority in this field in the U.S.[39]

"Dyspepsia (indigestion) is best described as a functional disease. Sometimes, it is called functional dyspepsia. The concept of functional disease is particularly useful when discussing diseases of the gastrointestinal tract. The concept applies to the muscular organs of the gastrointestinal tract-esophagus, stomach, small intestine, gallbladder, and colon. What is meant by the term, functional, is that either the muscles of the organs or the nerves that control the organs are not working normally, or, as a result, the organs do not function normally. The nerves that control the organs include not only the nerves that lie within the muscles of the organs but also the nerves of the spinal cord and brain".

This is a traditional outlook on functional dyspepsia as a problem with hollow gastrointestinal organs that look like sacs or tubes (esophagus, stomach, small intestine, gallbladder, and colon) without even focusing on the solid digestive organs such as the pancreas and liver.

It is the opinion of the authors, that the pancreas and liver (the vital digestive glands that produce bile and pancreatic juice) play a major role in the development of functional digestive disorders.

Symptoms from the hollow gastrointestinal organs are the consequences of improper functioning of the pancreas, liver, and bile (for methodological purposes bile will be referred to as an organ). Functional changing in the biochemistry of bile and pancreatic juice leads to the decreasing of exocrine pancreatic function and indigestion, which the authors refer to as *acidic pancreas and bile*. This, in turn, may cause many digestive symptoms, which are related to Functional Gastrointestinal Diseases.

e. Functional Dyspepsia, Irritable Bowel Syndrome, and the Pancreas

In 1987, Doctor H. Worning from the University of Copenhagen, Denmark wrote in *Digestion* that the prevalence of pancreatic diseases as the cause for dyspepsia differs in clinical materials between 0 and 25-30%. In his view, pancreatic function and pancreatic disease are connected to

different gastro-intestinal diseases (duodenal ulcer, inflammatory bowel diseases, malabsorption syndromes, subtotal and total gastrectomy and to some extent in patients with hepatobiliary diseases).[132]

Japanese doctors Okada R *et al*. (2009) considered that mild functional pancreatic disorders might trigger some cases with unexplainable chronic dyspepsia.[130]

Eva Lindström *et al*. (1990) from Sweden suggested that altogether, 66% of the patients with abdominal pain had morphological and/or functional evidence of pancreatic affection.[131]

Some researchers agree that differentiation between functional dyspepsia and early chronic pancreatitis is difficult.[124] Early stages of chronic pancreatitis and decreasing of exocrine pancreatic function are commonly misdiagnosed.

According to the *Second Giessen International Workshop on Interactions of Exocrine and Endocrine Pancreatic Diseases* in 2008, "Early chronic pancreatitis remains a diagnostic challenge as there is no gold standard for the diagnosis and pancreatic biopsy is risky and impractical. Reported data on the incidence and prevalence of chronic pancreatitis are unreliable and highly variable. Chronic pancreatitis is clearly under – diagnosed"[51]

Smith *et al*. (1991) reported abnormal Lundh tests in 27% of patients where conditions were classified as "functional dyspepsia." The Lundh test is used to estimate the pancreatic function. They concluded, "Pancreatic disease may explain the symptoms of some patients with non-ulcer dyspepsia"[121]

The diagnosis of the beginning of the pancreatic disorders might be missed in clinical practice because symptoms of severe exocrine pancreatic deficiency (malabsorption syndrome and maldigestion) are not specific in the early stages of chronic pancreatitis

As a result, early chronic pancreatitis is rarely suspected when pain is mild or absent and when symptoms are unspecific ("dyspepsia") in the absence of steatorrhea.

Irritable bowel syndrome (IBS or spastic colon) is a functional bowel disorder characterized by chronic abdominal pain, discomfort, bloating, and alteration of bowel habits in the absence of any detectable organic cause. In some cases, the symptoms are relieved by bowel movements. Diarrhea or constipation may predominate, or they may alternate.

There is no specific laboratory or imaging testing, which can be performed to diagnose irritable bowel syndrome. Diagnosis of IBS involves excluding conditions, which produce IBS-like symptoms, and then following a procedure to categorize the patient's symptoms.

Researchers have identified several non-gastrointestinal medical conditions, which appear with greater frequency in patients diagnosed with IBS, which include headache, fibromyalgia, chronic fatigue syndrome (CFS) and depression. A group of researchers from the Boston University School of Medicine, Boston, MA, USA, Cole JA *et al*. (2006) [133] studied 97,593 individuals with IBS identified comorbidities as headaches, fibromyalgia, and depression. A systematic review found that IBS occurred in 51% of CFS patients and 49% of fibromyalgia patients, and psychiatric disorders were found to occur in 94% of IBS patients.[134]

Bercik P. *et al*. (2005) suggested that IBS is a type of low-grade inflammatory bowel disease. [135] Researchers believe that IBS and Inflammatory Bowel Disease (IBD) are interrelated diseases, noting that patients with IBD experience IBS-like symptoms when their IBD is in remission. A 3-year study published in 2000 by García Rodríguez LA *et al*. (2000) found that patients diagnosed with IBS were 16.3 times more likely to develop IBD during the study period. [136]

Irritable bowel syndrome (IBS) has some of the same symptoms as gallbladder disease, including difficulty digesting fatty foods.[139]

A 2008 study found that IBS patients are at increased risk of having unnecessary cholecystectomy (gall bladder removal surgery) not due to an increased risk of gallstones, but rather due to abdominal pain, and the doctor being aware of the presence gallstones. [137] A 2005 study reported that IBS patients are 87% more likely to undergo abdominal and pelvic surgery, and three times more likely to undergo gallbladder surgery.[331]

A study published by Longstreth GF, Yao JF (2004) in *Gastroenterology* came to similar conclusions, and also noted that IBS patients were twice as likely to undergo hysterectomies. [138]

Today, there is not a common acceptable theory how the functional digestive diseases are developed. There is not much research about the important role of the pancreas – "the hostess of gastrointestinal tract" and bile in these diseases. The authors postulate that the acidifying of pancreatic juice and bile triggers IBS, and this common condition is a functional stage of exocrine pancreatic deficiency, which is referred to as *acidic pancreas and bile*.

f. Functional Dyspepsia, Irritable Bowel Syndrome, and the Bile

In a healthy situation, the liver produces the liver bile with a large amount of conjugated bile acids as the bile salts. The human organism uses these relatively non-toxic conjugated bile acids (bile salts) for digestion of fat and fat-soluble vitamins. When the bile becomes acidic, the composition of bile changes and there are more deconjugated (real) bile acids in the bile. These deconjugated bile acids are very aggressive acidic substances that irritate, corrode the small

intestine walls, induce inflammation and ulcers in the duodenum and cause spasms of the Sphincter of Oddi and bile reflux.

If the aggressive bile travels to the stomach or esophagus, it can cause irritation, inflammation, ulcers and even cancer. If the aggressive bile travels to the pancreatic duct, it can cause activation of the digestive pancreatic enzymes inside the pancreas and pancreatitis. Deconjugation of bile acids may be responsible for many symptoms of the small and large intestines.

In a healthy situation, the pancreas produces digestive pancreatic enzymes and bicarbonates. Pancreatic enzymes work only in an alkaline environment. This is why the pancreas produces a lot of bicarbonates to neutralize the acidic chyme, which comes from the stomach.

During chronic acidity, the body uses the minerals and bicarbonates to neutralize the acidity in the blood to promote the normal function of vital organs such as heart, brain and lungs for the price of pancreas and liver. Deficiencies of minerals and bicarbonates change the biochemistry of pancreatic juice and diminish or even stop the activity of pancreatic enzymes, causing abnormal digestion of food – indigestion (dyspepsia).

Acidic “aggressive” bile may cause Sphincter of Oddi dysfunction – the very common functional spasms of this muscle's valve regulating the moving of bile and pancreatic juice into the duodenum. Sphincter of Oddi Dysfunction type III symptoms are very similar to many functional digestive diseases and include cramps, spasmodic pain in the upper part of the abdomen, fullness, nausea, vomiting, bloating, etc.[129] Similarity, connections between Sphincter of Oddi Dysfunction and IBS are also emphasized.[43, 128]

For decades, the authors have strongly believed that many individuals with IBS actually suffer from indigestion due to the abnormal function of the pancreas and low quality of bile. Leeds JS *et al*. (2009) also considered that some patients with irritable bowel syndrome might have exocrine pancreatic insufficiency.[127]

Although irritable bowel syndrome (IBS) is not a life threatening disease, it can be terribly debilitating for those who suffer from this condition. IBS usually involves a group of recurring symptoms that may include fullness, abdominal cramps or pain, bloating, gas and excessive flatulence, nausea, stomach rumblings, diarrhea and/or constipation.

g. Patients with IBS may present one of three clinical variants:

1. Complaining primarily of chronic abdominal pain and constipation
2. Having a chronic intermittent diarrhea, often without pain
3. Having the features of both and complaining of alternating constipation and diarrhea

Lower activity of pancreatic enzymes, improper bile flow, and changed biochemistry of bile can cause the lower abdominal symptoms, flatulence, constipation, and diarrhea.

Insufficient amounts of digestive enzymes can cause or exacerbate abnormal digestive conditions, such as maldigestion, food allergies or sensitivities, intestinal fermentation, putrefaction, peroxidation, and the phenomenon known as increasing of intestinal permeability, or “leaky gut syndrome.”

The symptoms that associate with digestive weakness are:

> Indigestion and fullness lasting 2-4 hours after eating

> Bloating

> Excessive passage of gas

> Abdominal cramps and aches

> Difficulty gaining weight

> Roughage and fiber causing constipation

> Alternating constipation and diarrhea

> Undigested food and mucus in the stool[145, 146]

Biliary disorders can cause either constipation or diarrhea. In 1943, American doctor Harry Gauss from the University of Colorado described biliary constipation. Biliary constipation, which is caused by the reduced formation or flow of bile, occurs commonly in middle aged individuals with sedentary habits in whom there is present some form of biliary or hepatic disease, either functional or organic. Treatment consists of giving whole bile or bile salts.[143]

Gallbladder problems and constipation frequently go together. Constipation, light colored or chalky stools, pain or nausea after eating, difficulty digesting fats, gas and bloating, headaches, and a bitter taste in the mouth are all signs that gallstones or other gallbladder ailments have reduced the flow of bile.

Bile acid malabsorption is a syndrome of chronic watery diarrhea with excess fecal bile acids. It is known, bile mostly consists of conjugated bile acids (bile salts) and a very small amount of free bile acids. Disruptions of normal biochemistry of bile by metabolic acidosis lead to precipitation of free bile acids, which cause irritation of small and large intestines and finally diarrhea. Bile salts may be also inactivated in the intestinal lumen by overgrowth of bacteria in the Small Intestinal Bacteria Overgrowth syndrome.

Laurence Scott Bailen, M.D. from Tufts University stated in the *Open Course Ware Lecture* (2007), “Bile salts may be inactivated in the intestinal lumen by overgrowth of bacteria in the small bowel bacterial overgrowth syndrome. These excess bacteria deconjugate bile salts leaving them unconjugated and unable to participate in micelle formation. Deconjugated bile acids are toxic to the colonic epithelium and cause diarrhea. This leads to malabsorption of fat and

symptoms of abdominal pain, diarrhea, and bloating. It may also lead to malabsorption of the fat soluble vitamins A, D, E, K".[144]

In 1976, A.M. Weber *et al*. studied the relationship between bile acid malabsorption, diarrhea and pancreatic insufficiency. This group found that bile acid precipitation and malabsorption may be combined with some degree of pancreatic insufficiency. What is important, in terms of connecting this condition with metabolic acidosis, was that these researchers found that administration of bicarbonate led to a significant decrease in fat loss.[147]

The authors conclude that acidity, which causes bile acid precipitation, most likely plays a dominant role in the development of pancreatic steatorrhea in the end stage of exocrine pancreatic deficiency, which we refer to as *pancreatic failure*.

Most patients suffering from IBS also have the non-bowel symptoms such as fatigue, depression, lack of energy, headaches, muscle aches, slipping difficulties, lower back, and pelvic pain, which can be probably related to chronic metabolic acidosis, as well.

h. Functional Dyspepsia, Irritable Bowel Syndrome, and Dysbiosis

All these symptoms of IBS are very similar to the symptoms of intestinal dysbiosis (Candida-yeast overgrowth and/or Small Intestinal Bacteria Overgrowth), as well. This gave the idea for scientists to check the possible connection between these common conditions. Research conducted in Norway by Santelmann H. *et al*. and published in January 2005, suggested that *Candida* may be a cause of irritable bowel syndrome. They stated that " there is increasing evidence for yeasts being able to cause IBS-symptoms in sensitized patients".[41]

Collins SM *et al*. (2009) wrote that "Disruption of the delicate balance between the host and its intestinal microbiota (termed dysbiosis) results in changes in the mucosal immune system that range from overt inflammation as seen in Crohn's Disease, to low grade inflammation without tissue injury, as seen in a subset of IBS patients".[231]

Other published articles have implicated intestinal dysbiosis as contributing to IBS.[140, 141, 142]

The authors consider that gastrointestinal functional diseases, especially dyspepsia and IBS, are a consequence of a few conditions that interrelate and aggravate each other. They include consumption of acidic-forming food without natural living enzymes, dysbiosis (Candida-yeast overgrowth) and the toxic environment inside and outside the body.

These conditions all cause chronic acidity in the body – chronic metabolic acidosis, which negatively influences the alkaline digestive glands, such as the liver, which produces bile, and the pancreas that produces pancreatic enzymes and bicarbonates.

Metabolic acidosis, dysbiosis and inner toxicity diminish the exocrine pancreatic function, thus, causing many gastrointestinal symptoms.

The idea about a connection between the decreasing of pancreatic function and gastrointestinal functional diseases has a common pathophysiological sense and is supported by other research. [121, 127]

It is the opinions of the authors, that most of the functional digestive diseases are based on the functional deficiency of bile and the pancreas, which we clinically functionally classify as *acidic pancreas and bile*. Medical care must be taken to unravel the cause from its consequence. The lack of understanding the physiologic processes that cause dyspepsia and IBS has meant that treatment usually cannot be directed at the underlying mechanisms. Instead, treatment usually is focused on the symptoms but not the root of the problem with corresponding results.

Interesting facts at a glance:

More than half of Americans have digestion problems. Most of them have functional digestive disorders

Functional disorder testing is usually normal, however people suffer from symptoms of indigestion

Improperly digested foods commonly lead to nausea, vomiting, belching, heartburn, low appetite, abdominal cramps, and diarrhea/constipation

The most frequent functional gastrointestinal diseases are Dyspepsia and Irritable Bowel Syndrome (IBS)

There is overlap between functional dyspepsia and irritable bowel syndrome (IBS)

Dyspepsia or abnormal digestion of food is one of the most common illnesses, affecting an estimated 20% of individuals in the United States. Possibly, only 10% of those affected actually seek medical attention for their dyspepsia

Irritable Bowel Syndrome (IBS) is the number one digestive disease in America with 30-50 million sufferers. Some 22 % of the United States population has Irritable Bowel Syndrome (IBS) symptoms, either occasionally or persistently

Almost 35% of the world's population suffers from functional gastrointestinal disorders. 40% of those visit gastroenterologists and 12% visit primary care physicians

Almost half of patients with IBS have non-digestive symptoms such as headaches, depression, fibromyalgia, and allergies

A high amount of individuals don’t seek conventional medical care such as those that consider their symptoms “normal”, those that visit alternative medicine practitioners and those without medical insurances

Individuals with functional digestive disorders, dyspepsia and/or IBS, commonly have the symptoms from the hollow gastrointestinal organs (esophagus, stomach, small intestine, gallbladder and colon

Nevertheless, the origin of the functional digestive disorders is low pancreatic function and improper quality of bile

Interrelation of Metabolic Acidosis with the Lowering of Exocrine Pancreatic Function and Intestinal Dysbiosis causes decreasing of pancreatic digestive enzymes and improper quality of bile. This in turn produces a cascade of indigestion, irritations, refluxes (wrong way traffic), spasms and inner toxicity, which make the life of sufferers terrible

Symptoms of dyspepsia, IBS or early chronic pancreatitis are very difficult to distinguish. The beginning of chronic pancreatitis is commonly underdiagnosed

The lack of understanding of the physiologic processes that cause dyspepsia and IBS means that treatment usually cannot be directed at the underlying mechanisms. Instead, treatment usually is focused on the symptoms but not the root of the problem with corresponding results

The authors consider functional dyspepsia as the *acidic pancreas and bile* stage of exocrine pancreatic disorder and offer a healing program for this condition

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Chapter 15-Intestinal Dysbiosis: Candida-yeast Overgrowth and Small Intestinal Bacteria Overgrowth (SIBO)

For individuals lacking a medical background

Imagine the following picture: There is an "employer" (human body) and there is its "employee" (friendly intestinal flora). And they peacefully co-exist on the terms of a "contract." The flora perform the labor, and for this work, the human body repays the "employee" with shelter and food. Thus, it is clear that in default of the contract by the "employer", the "employee" revolts and leaves the body. However, the space previously occupied by the "employee" cannot remain empty. Other "unfriendly visitors", one of them being Candida-yeast, need and take this shelter and food. Since these unfriendly visitors cannot perform the job of "employee", they suck up the vitality of the host.

The modern person daily breaks "the contract on cooperation" with the friendly intestinal flora with the poor-quality food containing many harmful chemicals, the toxic substances inside and around the body, the disgusting ecological environment and stress. This all leads to dysbiosis (Candida-yeast overgrowth or Small Intestine Bacteria Overgrowth) and conducts to a "revolt" by the flora against the owner. But the most widespread reasons of dysbiosis are antibiotics, more precisely their uncontrolled use, and modern diet.

In the United States, it is very difficult to find an individual whom has not taken or ingested antibiotics, hormones, birth control pills, painkillers, foods with plenty of sugar, sweets, and processed ingredients, sodas, faucet water, alcohol, or one who has eaten only organic products. It is no wonder then that millions of Americans suffer from dysbiosis. During these conditions, the friendly intestinal flora is disrupted by any of the factors previously discussed, and without competition, the Candida-yeast and other "unfriendly visitors" take over the gastrointestinal tract.

The gastrointestinal tract harbors more than 400 species of microorganisms. Some scientists consider intestinal flora as another human organ, which is responsible for digestion, immunity, manufacturing and absorbing of vitamins and other essential substances, metabolism, detoxification of the body from the poisonous chemicals, and so on.

The "gut flora" in the gastrointestinal tract of the average individual consists of more than 400 species of bacteria, yeast, and other microorganisms numbering approximately 100 trillion in total. Normally, the weight of the bacteria inside an adult is about 2 kg (4-5 pounds), and the quantity of these microorganisms outnumbers the total number of cells in the human body by a ratio of 100 to 1. Fortunately, most of these organisms do not cause disease but, in fact, help protect the body from many diseases.

Researchers have told us for years that good health begins in the gut

The first who paid attention to human health and intestinal flora was the Great Russian microbiologist and 1908 Nobel laureate, Dr. Ilya Mechnikov. Dr. Mechnikov correctly observed that Bulgarian farmers lived longer than average and associated this with their intake of cultured, sour milks. He associated their rich diet of lactobacillus he named it *Lactobacillus Bulgaricus*, with increases in longevity, and found that such a diet curbed the abnormal growth of disease-causing bacteria in the intestinal tract. Dr. Ilya Mechnikov also coined the term "probiotic" to describe friendly bacteria that are essential "for life".

a. What Is Candida?

Candida, also known as *Candida albicans*, is the yeast commonly found in human bodies. Yeast prefers dark, moist, or humid places, whether it is in either on your body or in your basement. Since yeasts love warm, wet, dark places, yeast infection appears in places such as the intestines, vagina, throat or mouth. Yeast infection is fairly common now. Some researchers estimate that 80 million Americans suffer from chronic candidiasis (Candida-yeast infection).

Three kinds of microorganisms live in our body: friendly, unfriendly (harmful) and opportunistic. Candida-yeast, mostly *Candida Albicans*, is an opportunistic parasitic

microorganism that lives in almost everybody's digestive tract in tiny amounts and is a close relative to molds and fungus. Candida-yeast is referred to as an opportunistic microorganism because it overgrows and multiplies when it has the opportunity to do so. Shortly, Candida-yeast is an opportunistic infection that grows only when it has opportunity to grow, typically when the friendly intestinal flora is gone.

In normal conditions, Candida-yeast does not have this opportunistic chance because it is controlled by friendly intestinal flora. Even one round of antibiotics destroys the friendly intestinal flora, but does not kill the Candida-yeast.

You might remember that the antibiotic penicillin was manufactured from yeast-mold. Candida-yeast is resistant to almost all antibiotics. This is why yeast survives when these heavy drugs kill the gentle friendly intestinal flora. Without competition from friendly flora, Candida-yeast takes over the GI tract. From the beginning, Candida-yeast occupies the large intestine, than expands to the small intestine and later, in the worse scenario, inhabits the entire body.

The popular perception is that Candida-yeast overgrowth is the consequence of antibiotics usage. Many medical practitioners dismiss this as fantasy, saying that antibiotics could not have that effect in healthy individuals. But it may be that antibiotics act as the "straw that broke the camel's back" where health has already been compromised.

The simple example is the post-infectious irritable bowel syndrome (IBS). The majority of patients describe a precise time of the onset of post-infectious IBS following an attack of acute infections or an anti *H. Pylori* course treated by antibiotics. If any of these drugs are taken for infections, large numbers of the friendly bacteria such as lactobacilli and bifidobacteria are wiped out from the intestines. These friendly bacteria provide protection from other, potentially harmful, intestinal residents such as Candida-yeast and intestinal parasites.

Searching in online search engines such as Google may show the importance of these conditions for the world population. Here is how the search approximately looks:

Google's Key Words Results (in 2012)

Candida: 39,500,000

Candida-yeast: 3,000,000

As one can see by the Google search, Candida is not recently imagined. Many alarming scientific, statistical and clinical evidences increasingly show that nowadays, dysbiosis and especially Candida-yeast overgrowth - candidiasis, are considered serious medical, social and worldwide problems.

b. What is Dysbiosis?

If the human being and the microorganism live together in harmony, a healthy state of symbiosis results. Symbiosis is broken down into two parts: *Sym*- from the Greek meaning "together with" and *Bio* meaning “life”. In Biology, symbiosis is defined as “A close, prolonged association between two or more different organisms of different species that may benefit each member”.

The human host gives the friendly intestinal flora “room and board” and the friendly flora is so thankful that they perform many beneficial things for us, which include:

- Competing with harmful bacteria, yeasts and parasites, thus keeping them at harmless levels
- Promoting the digestion of food and efficient absorption of nutrients
- Producing digestive enzymes such as protease, lipase and lactase
- Helping to regulate the bowel movements
- Producing “natural” antibiotics, which inhibit the growth of dangerous infectious microorganisms
- Helping to regulate hormonal and cholesterol levels
- Stimulating the immune system
- Promoting to manufacture vitamins and anti cancer substances

Alternatively, dysbiosis (a contraction of the term “dys-symbiosis”, *dys*- meaning "bad, ill, abnormal") occurs when this balance is upset.

Dysbiosis can result from a deficiency of good bacteria and losing their health benefits. In addition, Dysbiosis is an overgrowth of harmful organisms such as Candida-yeast, parasites, or other harmful bacteria in the small and large intestines. In either case, this disordered “ecology within” often results in many diseases of not only the GI tract, but also the entire body

A dysbiosis is a complex environmental condition. It must urgently be treated. If left alone, it can be serious problem. Candida can change from a non-disease state to a disease-causing state and then produce root like structures called rhizoids that may penetrate the intestinal walls causing damage and holes. Yeast, toxic waste, bacteria, and undigested food may then enter or “leak” throughout these holes into the bloodstream which results in Leaky Gut Syndrome.

This causes severe allergies, bloating, skin rashes, painful and inflamed joints, muscle pain, brain fog and sinus problems.

William G. Crook, M.D., designed the following self-test to be used by adults to identify their predisposition to *Candida albicans* yeast infection.

Are YourHealth Problems Yeast Connected? By Dr. William G.Crook

If your answer is yes to any question, circle the number of points you've accumulated. Your score will help you determine the possibility (or probability) that your health problems are yeast connected.

Self – Test Point Score

1. Have you taken repeated or prolonged courses of antibacterial drugs? - **4**

2. Have you been bothered by recurrent vaginal, prostate, or urinary infections? - **3**

3. Do you feel "sick all over," yet the cause hasn't been found?. - **2**

4. Are you bothered by hormone disturbances, including PMS, menstrual irregularities, sexual dysfunction, sugar craving, low body temperature, or fatigue? - **2**

5. Are you unusually sensitive to tobacco smoke, perfumes, colognes and other chemical odor - **2**

6. Are you bothered by memory or concentration problems? Do you sometimes feel "spaced out"? - **2**

7. Have you taken prolonged courses of prednisone or other steroids; or have you taken "the pill" for more than 3 years? - **2**

8. Do some foods disagree with you or trigger your symptoms? - **1**

9. Do you suffer with constipation, diarrhea, bloating, or abdominal pain? - **1**

10. Does your skin itch, tingle or burn; or is it unusually dry; or are you bothered by rashes? - **1**

Scoring for women: If your score is **9** or more, your health problems are probably yeast connected. If your score is **12** or more, your health problems are almost certainly yeast connected.

Scoring for men: If your score is **7** or more, your health problems are probably yeast connected. If your score is **10** or more, your health problems are almost certainly yeast connected.

c. How Does Dysbiosis Effect Pancreatic Health?

If yeast, sugar, and wheat are placed in warm water, fermentation takes place and alcohol will be manufactured there. Typically, alcoholic beverages, such as beer, wine, and whiskey, are made from the controlled use of fermentation. In individuals with intestinal dysbiosis and Candida-yeast overgrowth (Small Intestine Bacterial Overgrowth), this process continues without control inside their bodies continuously without stop. During this fermentation, besides the breakdown of carbohydrates into carbon dioxide and alcohol, Candida-yeast produces many other toxic substances known as mycotoxins. One of these is acetaldehyde, a substance that is a poison to the body and especially the pancreas.

The human intestinal tract harbors both friendly and unfriendly microorganisms. Years of antibiotic and pill usage, stress, the excessive consumption of processed food, sugar and alcohol and drinking chlorinated water knocks out the normal friendly bacteria while they are fighting

off enemies. Prescriptions for antibiotics are not the only source of concern: antibiotics have been added to domestic animal feed since the 1950s.

Yeast is great for bread making because it gobbles up the sugar that is added to it. This makes a big, puffy, gassy mess that gets larger as flour is added. This is essentially the way the yeast – afflicted patients usually feel: like bread. Patients feel bloated, puffy, and distended especially after eating sweets and starchy food.

Candida-yeast overgrowth can be described as a condition that acts as a chameleon by changing its appearance frequently and rapidly. It can manifest itself in many forms and mimic many diseases of any kinds of organs or systems. Everyone can be a victim of Candida-yeast overgrowth, whether they are old or young, male or female. Individuals may experience conditions such as sinusitis, nose bleeds, bladder infections, fatigue, thyroid dysfunction, bad breath, dry cough, hemorrhoids, constipation, IBS, burning and ulcerated tongue, bruising, damaged intestinal walls (leaky gut syndrome), acne, vaginal infections, premenstrual syndrome (PMS) and prostatitis.

Yeast gives off toxins, which weaken the immune system and cause fatigue, allergies, depression, digestive disturbances, infections, sex problems, memory loss and "feeling sick all over". (See patient profile).

d. Typical Chronic Candidiasis Patient Profile

Sex: Females are affected more than males

Age : 15-60

General Symptoms:

> Chronic fatigue

> Allergies

> Chronic infections (repeated sinusitis, ear infection, UTI, acne)

> Many respiratory infections (constant dry cough, frequent colds, flu)

Gastro-Intestinal symptoms:

> Craving for sweets

>Gas, bloating, heartburn, cramps and indigestion

> Intermittent constipation or diarrhea

> Bad breath and mouth thrush

> Food allergies and food sensitivity

> Rectal itching

Genito-Urinary symptoms:

> Recurrent vaginal yeast-infection

> Frequent bladder infection

> PMS

> Prostatitis

Nervous System symptoms:

> Depression and mood swings

> Irritability, poor memory and headache

> Inability to concentrate

Musculoskeletal symptoms:

> Fibromyalgia

> Joint pain

> Neck, shoulder and back pain after exercises (repairing deficit)

Skin symptoms:

>Itching, rashes, and dry skin

>Eczema and dermatitis

>Acne

>Rosacea

Hormonal System symptoms:

> Low adrenaline (chronic fatigue, low immunity)

> Low thyroid (cold hands and feet, low BP, low body temperature, puffy face)

> Insulin resistance, hypoglycemia attacks, and hyperglycemia

> Infertility, changes in the menstrual cycle and decreased libido

Past history:

> Multiple antibiotics use

> Birth-control “pills”

> Prednisone use

> History of food poisoning or parasites

> Alcohol abuse

If the friendly bacteria are disrupted by any of the factors previously discussed, Candida can increase its numbers drastically and become a more dominant member of the "intestinal jungle".

e. Candida-yeast overgrowth can totally disrupt digestion in many ways such as:

I Influencing yeast metabolites directly on pancreatic function and digestive enzymes with toxins

II. Causing chronic body acidity

III. Promoting Leaky Gut Syndrome

IV. Decreasing Immune system function

V. Promoting Small Intestine Bacterial Overgrowth (SIBO)

I. Toxic Yeast Metabolites Directly Influence on Pancreatic Function and Digestive Enzymes

Candida-yeast overgrowth causes severe inner poisoning of the body. Yeast secrets the mycotoxins, which are very toxic for the nervous and hormonal systems. This can explain the "brain fog", fatigue, fibromyalgia, depression, adrenal and thyroid problems, PMS and overweight issues in individuals with dysbiosis. Candida-yeast overgrowth constantly produces inner alcohol in the body. Alcohol has an ability to enhance the toxicity of most common drugs and other toxins. Acetaldehyde is considered to be the most toxic of alcohol by-products. It is the substance, which gives us the feeling of having a 24/7 hangover. Anybody who has experienced a morning hangover can tell you how awful he or she felt that way.

There is evidence that Candida-yeast overgrowth directly can cause acute and chronic pancreatitis. Candida can inactivate the pancreatic digestive enzymes, thus cause indigestion and problems with absorption of essential nutrients such as vitamins and minerals. A deficiency of these vital nutrients, in its turn, decreases the amount and activity of pancreatic digestive enzymes causing a "vicious circle". In healthy conditions, the pancreatic protease – the enzyme that digests the protein, kills the harmful bacteria and yeast. When the activity of protease decreases, our body loses one of its very important defense mechanisms and becomes vulnerable to Candida-yeast overgrowth too. This is an example of another "vicious circle" caused by Candida.

The main harbor for Candida is the large intestine. It usually leads to colon spasms, constipation, diverticulosis, hemorrhoids, gas, excessive flatulence, bad body odor and headaches. On the other hand, friendly intestinal flora cannot survive during chronic constipation. Constipation creates an inner environment for multiplying of Candida-yeast and other unfriendly bacteria, causing rotting and inner toxicity.

II. Causing Chronic Body Acidity

The modern diet, especially the “Standard American Diet” (S.A.D.), includes plenty of sugar, white flour and sodas, which is the excellent environment for multiplying of yeast and constant fermentation. It is known that yeast carries out fermentation in the production of ethanol in beers, wines and other alcoholic drinks, along with the production of large quantities of carbon dioxide.

During the process of fermentation, many acidic products are formed in the body. This leads to a chronic acidic condition – chronic metabolic acidosis. There is evidence about direct harmful action of the toxic acidic substances from yeast fermentation such as alcohols or aldehydes on the pancreas.

III. Promoting Leaky Gut Syndrome

Think of your gut as a one-way fence. The inner lining of the gut is porous. Normally, small particles of digested food are able to pass through the holes of the intestinal lining into the blood. After that, nutrients from food can reach the cells. In a healthy body, these "holes" are small enough to keep large molecules, which might otherwise cause harm from going into the blood system. Therefore, the organism protects itself from the intestinal toxic load and microorganisms travel into the blood system.

Leaky gut syndrome is one of a number of disorders associated with increased intestinal permeability, where the one-way gates of the gut, in effect, open too wide. Normally, the larger the molecule, the less likely it is to be allowed across the gut. Once the gut lining becomes inflamed or damaged, it becomes more difficult to keep foreign, larger particles out. As the spaces between intestinal cells open up, larger particles are allowed to be absorbed into the body such as undigested food, microorganisms, parasites and toxic substances.

Increased gut porous may play a primary role in causing many diseases. Increased gut permeability may be a consequence of many diseases too. This causes immune system reactions, pancreatic deficiency, liver dysfunction, and food indigestion. In most cases, the role of increased intestinal permeability often goes unrecognized.

Today, Leaky Gut Syndrome is a very common condition. The key and most common causes of this syndrome are dysbiosis, and Candida-yeast overgrowth with subsequent chronic irritation and inflammation of the guts’ walls. Candida is a yeast-fungal organism that grows roots like a plant. These roots grow into and through the lining of the intestinal tract searching for food. These roots break through the intestinal lining and make the spaces between the cells of the gut wall. These spaces are holes in the gut wall through which "foreign" materials (large particles of improperly digested food, bacteria, parasites, and toxins) leak into the body and place an additional burden on the immune and detoxification systems.

IV. Decreasing Immune System Functions

The gastrointestinal tract is the largest immune organ in the body. The intestinal lining has a huge surface area that separates the external world from the internal milieu of the body. This intestinal lining is the ideal strategic location for potentially dangerous chemicals and organisms to enter. If this large, strategically placed immune system isn't working properly, that the lowered immune defenses will not be sufficient to keep the ecology of the intestinal tract in balance.

Whenever this intestinal barrier is damaged in any way, incompletely digested food particles, microorganisms, and toxins slip through the gut's wall. The body recognizes these substances as foreign and forms allergic responses to them, which is why individuals suddenly become allergic to foods they have always eaten without a problem. Food allergies have a negative impact on the work of the pancreas. In the worst case scenario, food allergies can cause a deficiency of digestive pancreatic enzymes or even acute inflammation of the pancreas.

On the other hand, many patients with low pancreatic function have food allergies and sensitivities. Food allergies occur because the large food protein molecules are unable to be broken down by the digestive system due to the lack of pancreatic digestive enzymes. Low pancreatic function plays a major role in many cases of food allergies, particularly if a person has multiple allergies. Candida-yeast overgrowth and Leaking Gut Syndrome lead to many allergic reactions to food and development of autoimmune disorders.

V. Promoting Small Intestine Bacterial Overgrowth (SIBO)

In many cases of severe dysbiosis, there is also Small Intestinal Bacterial Overgrowth (SIBO). Because of the ability to better diagnose it, SIBO has been taking a lot of attention within the medical community for the last decade.

Small Intestinal Bacterial Overgrowth (SIBO)

For individuals lacking a medical background

In many cases of dysbiosis, there is a combination of Candida-yeast overgrowth and Small Intestinal bacterial Overgrowth (SIBO). Candida-yeast is a usual resident in the GI tract in many healthy people and starts to cause health problems only if there is the opportunity to multiply. To detect overgrowth, special tests that rarely are used in common practice, are necessary. Thanks to technology, noninvasive breathing tests may diagnose bacterial overgrowth in the small intestine. This is a possible reason that doctors have focused on SIBO the last decade.

Many factors can lead to bacteria and/or Candida-yeast overgrowth in the small intestine. This often causes problems for digestion and thus, the entire body

The digestion occurs mainly in the small intestine, in a narrow tube about 7 meters (23 feet) long and 1-1.5 inches in diameter. Almost all digestion occurs in this tube. Mather Nature doesn't like to feed invaders, so the amount of bacteria at this location very low. It must be emphasized again that the small intestine is designed for digestion, and that microbes and yeast are not allowed access. Otherwise, harmful invaders would eat our food and nutrients and starve us.

Just a tiny amount of friendly intestinal flora (lactobacilli) resides in the beginning of the small intestine - duodenum. Hence, in healthy conditions, the amount of microorganisms in the small intestine is very low.

f. Control of Microorganisms in the GI tract

All microorganisms and parasites, which we can obtain from food and water, travel to the stomach. The first strong guard of the GI tract; gastric acid, kills many microorganisms. Stomach acid serves as a barrier against bacteria. Because extreme acidity in the stomach kills the germs, little can survive passage through this hostile environment. When the acid is suppressed, however, bacteria, yeast, and parasites may travel through, thrive, and cause trouble.

Some of the invaders, which survive in the stomach, travel into the duodenum – the beginning of the small intestine. When the acidic gastric chyme escapes into the duodenum, a flow of bile is released from the gallbladder, while simultaneously, the pancreas releases the pancreatic juice. Here the semi-fluid digested food from the stomach is neutralized by pancreatic juice and bile, which are extremely alkaline in nature.

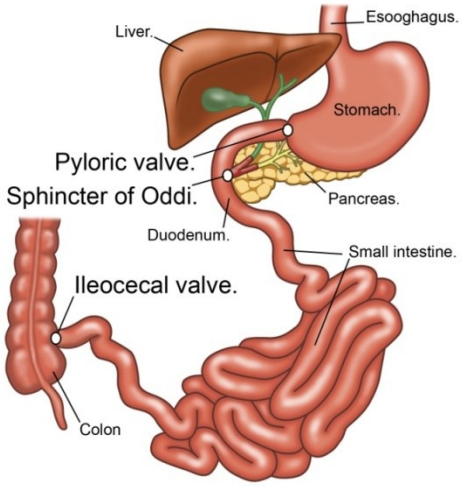
Pancreatic juice contains very strong antimicrobial substances. The enzymes that are designed to digest the proteins also digest unwanted visitors such as microbes, yeast, viruses, and parasites. Antimicrobial action of pancreatic juice makes the environment inside the small intestine clear and unfriendly for microbes and yeast. On the other hand, antimicrobial action of pancreatic juice also has a self-defense mechanism by killing the unfriendly bacteria. This process prevents infections of the pancreas and bile system by restricting bacteria from travelling through the duodenum to the pancreatic duct and gallbladder.

In healthy conditions, there is a minimum possibility for the survival of microorganisms in the small intestine. 2.5 quarts of bile and pancreatic juice plus about 2 quarts (1.8 liters) of intestinal juice are secreted into the small intestine each day. This "river" flashes out the unfriendly bacteria out of the small intestine, as well.

The intestinal mucosa produces secretions that primarily contain mucus, electrolytes, and water that enter the small intestine. This liquid mass moves fast through the small intestine. The unfriendly bacteria do not have the possibility to attach to the intestinal wall. High flow rates

make it difficult for bacteria to colonize the small intestine because they get washed out very quickly.

This small intestinal tube has three openings – three gates. Why are these three gates mentioned? Because of bacteria, yeast and parasites can enter into the small intestine only through these three openings.



One gate is at the beginning of the small intestine (duodenum). There is a muscle valve that is called the pyloric valve. Semi-digested food from the stomach goes throughout this opening into the duodenum.

Second gate is the Sphincter of Oddi – the opening in the duodenum where the pancreatic juice and bile go in the small intestine.

Third gate is located at the very end of the small intestine (ileum). There is a valve - the ileocecal valve that connects it to the first part of the large intestine (cecum). The ileocecal valve has two main functions. The first is to prevent the backflow of fecal contents with bacteria and yeasts from the colon to the small intestine. The second is to prevent the contents of the ileum from passing into the large intestine prematurely.

If all gates work properly, there is no overgrowth of bacteria or yeast in the small intestine

The healthy immune system fights and kills the unfriendly microorganisms inside the small intestine.

g. How Does Small Intestinal Bacterial Overgrowth (SIBO) Occur?

It can be easy to understand the reasons that lead to Small Intestine Bacterial Overgrowth – SIBO.

If the stomach acidity is decreased, the exocrine pancreatic function and antibacterial action of pancreatic juice is diminished, the ileocecal valve opens, our immune system is weak, or the

friendly intestinal flora is killed, then the small intestine receives the harbor of microbes, viruses, yeast and parasites.

These microorganisms:

- Eats our food and causes a deficit of vital nutrients

- Allows toxins to kill our body

- Enables these toxins to break the protective barrier of our GI tract, and run through intestinal walls to the blood and lymph and gain access to the rest of the body

- Causes chronic immune reactions such as allergies and autoimmune diseases

The stomach of a person with SIBO looks like a balloon because of continuous fermentation and gas production in the small intestine.

Another serious problem occurs when the secretion and antimicrobial activity of pancreatic juice is diminished. The small intestine is designed for digestion and not allowing access to the microbes and yeast. Otherwise, harmful invaders would eat our food and nutrients, thus, starving us. Thanks to human physiology, pancreatic juice contains very strong antimicrobial substances. One of them is trypsin; the enzyme that is designed to digest the proteins from food. Trypsin digests uninvited visitors such as microbes, yeast, viruses, and parasites, as well. Antimicrobial action of pancreatic juice makes the environment inside the small intestine clear and unfriendly for microbes and yeast. Trypsin also kills the unfriendly bacteria to prevent infection of the pancreas and bile system.

Producing and releasing a normal amount of good quality bile and pancreatic juice is vital to fight Candida-yeast overgrowth and Small Intestine Bacterial Overgrowth

All of the above may happen in Candida-yeast overgrowth and Small Intestine Bacterial Overgrowth (SIBO). The main reasons causing these overgrowths are overusing antibiotics, eating the Standard American Diet and stress. In this situation our best protector - the friendly intestinal flora, is diminished, and harmful microorganisms such as Candida-yeast and other opportunistic infections reside in the GI tract.

Dysbiosis is the pandemic condition; this is our price for progress, a stressful life, the toxic chemical environment inside and outside us and for believing that we are smarter than nature.

For individuals with medical backgrounds

Candida (*Candida albicans*) is the medical paradox of our times. The symptoms of yeast overgrowth target close to 80 million Americans each year and about 70% of these are women. Approximately every third woman in US has a history of vaginal yeast –infection and does not realize that it is the symptom of Candida-yeast overgrowth in the whole body.

Some health practitioners believe Candida-yeast infects as many as 89% of U.S. citizens, and needs to be treated first. On the contrary, other health practitioners appear reluctant to acknowledge it. Some doctors and health practitioners consider that Candida is a disorder that can only combine with other diseases such as AIDS.

h. Candidiasis

Candidiasis or thrush is a fungal infection (mycosis) of any of the Candida species, of which *Candida albicans* is the most common. Candidiasis encompasses infections that range from superficial, such as oral thrush and vaginitis, to systemic and potentially life-threatening diseases. Candida infections of the latter category are also referred to as candidemia and are usually confined to severely immunocompromised persons, such as those with cancer, individuals after organ transplants and AIDS patients. Superficial infections of skin and mucosal membranes by *Candida* causing local inflammation and discomfort are however common in many human populations.[154] While clearly attributable to the presence of the opportunistic pathogens of the genus *Candida*, candidiasis describes a number of different disease syndromes that often differ in their causes and outcomes. Commonly referred to as a yeast infection, it is also technically known as *candidosis, moniliasis*, and *oidiomycosis*.

The Infectious Diseases Society of America (IDSA) Standards and Practice Guidelines Committee (SPGC) convened experts in the management of patients with candidiasis. For the 2009 update, the Expert Panel completed the review and analysis of data published since 2004 in the published *Clinical Practice Guidelines for the Management of Candidiasis: 2009 Update by the Infectious Diseases Society of America.* [153] http://guideline.gov/content.aspx?id=14174

The panel of experts agreed that infections due to the Candida species are the most common of the fungal infections. Candida species produce a broad range of infections, ranging from nonlife-threatening mucocutaneous illnesses to invasive process that may involve virtually any organ. Such a broad range of infections requires an equally broad range of diagnostic and therapeutic strategies. This document summarizes current knowledge about treatment of multiple forms of candidiasis and is the guideline of the Infectious Diseases Society of America (IDSA) for the treatment of candidiasis.[153]

Invasive candidiasis is largely a disease of medical progress, reflecting the tremendous advances in health care technology over the past several decades. The most frequently implicated risk factors include the use of broad spectrum antibacterial agents, use of central venous catheters, receipt of parenteral nutrition, receipt of renal replacement therapy by patients in ICUs, iatrogenic neutropenia, use of implantable prosthetic devices, and receipt of immunosuppressive agents (including glucocorticosteroids, chemotherapeutic agents, and immunomodulators).

Candidemia is the fourth most common cause of bloodstream infections in the United States and in much of the developed world. Invasive candidiasis has a significant impact on patient outcomes, and it has been estimated that the attributable mortality of invasive candidiasis is as high as 47%, although many authorities estimate the attributable mortality to be 15%–25% for

adults and 10%–15% for neonates and children. The estimated additional cost of each episode of invasive candidiasis in hospitalized adults is $40,000.[153]

Candida, also known as *Candida albicans*, is opportunistic yeast that normally inhabits the mouth, throat, intestines, and genitourinary tract of most humans and is usually considered to be a normal part of the intestinal flora (the organisms that coexist with us in our digestive tract). In a healthy person, a properly functioning immune system and “friendly” intestinal bacteria control *Candida albicans*.

However, if the number of friendly bacteria is decreased, the immune system is weakened and conditions for yeast proliferation occur. *Candida albicans* cells undergo a profound metamorphosis and will shift from yeast to mycelial fungal form and start to invade the body. In a fungal state, it is invasive and can produce rhizoids, very long root-like structures. Rhizoids can penetrate mucosa or intestinal walls, leaving microscopic holes and allowing toxins, undigested food particles, bacteria and yeast to enter the bloodstream. This condition is known as Leaky Gut Syndrome and, in many instances, is an explanation for food and environmental allergies. When the condition becomes systemic, it can penetrate every organ it settles in, such as the lungs, mouth, lymphatic system, mouth, urinary tract and even the toenails. Candida-yeast produces, as a waste product, over 75 toxic substances that may poison the body. These conditions are generally referred to as candidiasis or Candida-Related Complex (CRC).

i. Why Are Dysbiosis and Candida-Yeast Overgrowth Prevalent Conditions in the Modern World?

Here is the list of primary common factors, which decrease the amount of friendly intestinal flora, weaken the immune system, and promote the abnormal growth of Candida in the body.

> Antibiotics: Overusing and repeated use of antibiotics reduce the number of "friendly bacteria" in the intestinal tract, which normally keeps the *Candida albicans* under control. The people can obtain antibiotics not only from medical prescriptions but also by eating meat and drinking milk or even water.

> Other Medications: According to Dr. Leo Galand, MD, F.A.C.P, using steroid hormones, immunosuppressants, and anti-inflammatory drugs, ulcer medications or acid blockers used for prolonged periods also have the same actions as antibiotics.[42]

> Toxic Metals and Chemicals Outside and Inside the Body: Toxic metals, such as mercury and other heavy metals such as lead and cadmium and chemicals such as aspartame, MSG and others can kill friendly intestinal flora, alter immune responses and allow yeast to proliferate. Many of these toxic substances from the home, garden, and workplace find their way into the intestinal tract through food, water, air and the skin.

> Immune Deficiency: Any condition that results in a weakened immune system can cause Candida proliferation. Candida-yeast overgrowth is often a complication of immune compromising conditions such as cancer, AIDS, chemotherapy and taking immunosuppressants, steroids, disease-modifying antirheumatic drugs and immunosuppressive drugs after organ transplants.

> Hormonal Imbalance: Hormonal balance is necessary for support of friendly flora in the gut. Pregnancy, use of birth control pills, low adrenals and thyroid disorders can all be causative factors of hormonal imbalances. Birth control pills are composed of progesterone-like hormones that, in addition to their intended use, alter the vaginal mucosa allowing Candida albicans to overgrow. Increased progesterone is also released during pregnancy, which accounts for the frequent vaginal infections many women experience at that time.

> Excessive Stress: Stress can induce significant alterations in gut microbiota, including a significant decrease in beneficial bacteria such as Lactobacilli and Bifidobacteria and an increase in Candida –yeast overgrowth and other opportunistic infections. These changes may be caused by the effects of stress hormones or by stress-induced changes to GI tract motility and secretions. [155]

> Diet: The composition of the diet has been shown to have a significant impact on the content and metabolic activities of the human intestinal flora. Some diets promote the growth of beneficial microorganisms, while others promote activity of intestinal microflora that can be harmful to the host. Diets high in processed carbohydrates (bread, pasta, white rice, sodas) and sugar can lead to Candida-yeast overgrowth. Overeating causes indigestion of food and allows fermentation.

> Alcohol: Alcohol kills friendly bacteria, increases toxic overload of the liver, diminishes anti bacterial pancreatic function, immunity and in turn allows Candida-yeast to grow.

> Chronic Constipation: Constipation either causes or is a consequence of the Candida-yeast overgrowth.

j. What Do Dysbiosis and Candida-Yeast Overgrowth Cause in the Human Organism?

Many investigators suggest that an intestinal overgrowth of *Candida albicans* (and other intestinal yeast) may be involved in several diseases such as IBS, food allergies, migraine headaches, asthma, indigestion and gas, chronic fatigue, depression related to PMS and vaginal yeast infection. The major causes of dysbiosis include poor diet/nutritional status, stress, antibiotic/drug therapy, decreased immune status, decreased gut motility, maldigestion, presence of toxicity.[42]

It is no wonder then, as the entire body is effectively "poisoned" by an overgrowth of Candida, which the numbers of symptoms it can produce are huge and this affects every organ and system of the body. Candida-yeast overgrowth leads to fermentation in the bowels because the yeast cells greatly prefer fermentation as long as sugars and starches are readily available for consumption.

Candida-yeast overgrowth is characterized by *"feeling sick all over."* Fatigue, allergies, immune system malfunction, depression, chemical sensitivities, mood swings, mental fatigue, urinary or vaginal infections, arthritis, IBS, spastic colon, PMS or craving for sweets or carbohydrates and digestive disturbances (constipation, diarrhea, bloating and abdominal pain) are just some of the symptoms.

In addition, 79 different toxic products released by *Candida albicans* place a considerable burden on the immune system. These toxins get into the bloodstream and travel to all parts of the body where they may cause a host of adverse physical, mental, and emotional symptoms.

Women are more susceptible for Candida overgrowth than men. This is related to the female sex hormone progesterone, which is elevated in the last half of the menstrual cycle. Statistics indicate that one in every three individuals living in the Western world has some form of *Candida albicans*. Almost every third woman in the United States has a history of a vaginal yeast infection in her life, and many men suffer from chronic yeast prostatitis without knowing about it.

According to Pezzilli, R., in his 2009 article *Chronic pancreatitis: Maldigestion, intestinal ecology and intestinal inflammation* printed in the *World Journal of Gastroenterology* [175], dysbiosis also might give rise to bile acid malabsorption and changes in intestinal permeability. Another name of the intestinal permeability disorder is Leaky Gut Syndrome.

Toxins released from *Candida albicans* proliferation cause symptoms of Candida overgrowth. Not all listed symptoms will occur in all individuals. Usually, approximately 20 symptoms will be present. (Underlined symptoms are most common).

k. Undetected Candidiasis

Many individuals can suffer from candidiasis and never even know it. Candida may be the underlying cause of chronic illness, bringing about a wide range of seemingly unrelated or intermittent symptoms and clinical disorders of varying magnitude that defy the diagnosis. All of these responses make a positive diagnosis of candidiasis frequently difficult. However, recurrent and common symptoms of CRC (Candida Related Complex) do exist and fall into the following different categories:

> **Gastrointestinal**: bad breath (halitosis), bloating, foul flatulence, coating on tongue (oral thrush), nausea, abdominal spasms, constipation, diarrhea, dry mouth, gas, heartburn, indigestion, inflammation, irritable bowel syndrome, obesity or/and excessive weight loss

> **Psychological** and **Allergic**: acne, bronchitis (recurrent), numbness, burning or tingling, chemical sensitivity, chest pain, coughing, earaches, hay fever, headaches, hives, muscle aches and tension, nasal congestion, persistent dry cough, sinusitis and sore throats, head tension and painful, swollen and stiff joints

> **Emotional** and **Mental**: ADD, ADHD, anxiety, disorientation, drowsiness, fatigue, low energy, mental confusion, mood swings between depression and irritability, hyperactivity, inability to concentrate, insomnia, irritability, muscle pain, muscle weakness, nervousness, poor memory and tingling and numbness

> **Hormonal**: Adrenal or thyroid gland dysfunction, cold hands or feet, low body temperature, hypoglycemia, hyperglycemia (diabetes), impotence, menstrual irregularity, infertility, loss of sexual feelings and PMS

> **Skin**: Acne, itchiness of the skin, anal itch, athlete's foot, dandruff, dermatitis, diaper rash, dry skin, eczema, excessive perspiration, facial rash, fungous infection of the nails, hives, impetigo, jock itch, possible lupus and psoriasis

> **Genitourinary**: Bladder infection (recurrent), burning on urination, frequent urination, cramps, cystitis (inflammation of the bladder), endometriosis (irregular or painful menstruation), fluid retention (edema), menstrual irregularities, painful intercourse, recurrent vaginal yeast infections, prostatitis, infertility, vaginal burning, itching or discharge.

l. Small Intestine Bacterial Overgrowth (SIBO)

For individuals with medical backgrounds

There is information about Small Intestinal bacterial Overgrowth (SIBO) from an abundance of articles of very respectful professors, MDs, PhD's from the USA and all over the world.

Andrew C. Dukowicz, MD, Brian E. Lacy, PhD, MD, and Gary M. Levine, MD from the Dartmouth Medical School and the Section of Gastroenterology and Hepatology at the Dartmouth-Hitchcock Medical Center, Lebanon, NH, USA wrote:

"Small intestinal bacterial overgrowth (SIBO), defined as excessive bacteria in the small intestine, remains a poorly understood disease. Initially thought to occur in only a small number of patients, it is now apparent that this disorder is more prevalent than previously thought. Patients with SIBO vary in presentation, from being only mildly symptomatic to suffering from chronic diarrhea, weight loss, and malabsorption.
A number of diagnostic tests are currently available, although the optimal treatment regimen remains elusive.
A common misconception is that SIBO affects only a limited number of patients, such as those with an anatomic abnormality of the upper gastrointestinal (GI) tract or those with a motility disorder. However, SIBO may be more prevalent than previously thought. This apparent increase in prevalence may have occurred, in part, because readily available diagnostic tests have improved our ability to diagnose SIBO".[246]

Oren Zaidel, M.D. and Henry C. Lin, M.D. from the Division of Gastroenterology, Department of Medicine, Cedars-Sinai Medical Center, Los Angeles, California, USA stated:

"Small intestinal bacterial overgrowth (SIBO) is an often-neglected mechanism for impaired nutrition.
The dramatic changes in the bacterial flora of the small bowel that occur in SIBO have a multitude of effects on nutritional status. The bacterial flora may compete with the host for critical nutrients, alter host metabolism, directly damage the absorptive mucosa of the host, and produce gastrointestinal symptoms that reduce or alter food intake by the host.
Multiple factors defend against SIBO and determine both numbers and types of bacteria found in the small intestine. The major defensive factor is normal small intestinal motility. Other defensive mechanisms involve mucosal immunity, intestinal, pancreatic and biliary secretions, and the ileocecal valve.

When bacteria enter the gut from the mouth, many ingested bacteria are killed in the acidic environment of the stomach
Both diet and antibiotic usage further affects the normal enteric flora".[247]

John K. DiBaise, M.D., Professor of Medicine, Mayo Clinic, Scottsdale, Arizona, USA emphasized:

"Small intestinal bacterial overgrowth (SIBO) is an increasingly recognized cause of malabsorption and is likely an under-recognized cause of a variety of nonspecific gastrointestinal symptoms. Disturbances in small bowel motility and gastric acid secretion are the principal predisposing factors providing a clue to patient groups at risk of this condition".[163]

The causes and conditions, which are connected to SIBO

Structural/Anatomic

- Surgeries on the stomach or/and small intestine
- Surgically created blind loops
- Small intestine diverticula
- Small intestine strictures (radiation, medications, Crohn's disease)
- Resection of ileocecal valve

Organ System Dysfunction

– Cirrhosis
– Renal failure
– Pancreatitis
– Immunodeficiency states
– Crohn's disease
– Celiac disease
– Malnutrition

Motility Disorders

– Gastroparesis
– Small bowel dysmotility
– Celiac disease

Metabolic Disorders

–Diabetes

– Hypochlorhydria

Elderly

Medications

– Recurrent antibiotics

– Gastric acid suppression

The causes and conditions, which are connected to SIBO are presented in the above. They are adopted from "*Small Intestinal Bacterial Overgrowth: A Comprehensive Review*" by Andrew C. Dukowicz, MD, Brian E. Lacy, PhD, MD, and Gary M. Levine, MD (2007).[246]

The most common symptoms of SIBO include abdominal cramps and discomfort, gas, bloating, and flatulence especially after consumption of carbohydrates. Features associated with micronutrient deficiencies (Vitamins B12, A, D and E, iron, thiamine, nicotinamide) also may be present. In severe cases, symptoms such as malabsorption, diarrhea, steatorrhea and weight loss are prevalent.

It is the opinion of the authors that these symptoms are very similar to symptoms of *pancreatic deficiency* and *pancreatic failure* stages of exocrine pancreatic deficiency.

Ironically, many researchers agree that antibiotics can cause Small Intestinal Bacterial Overgrowth (SIBO) and that the conventional treatment of this condition is taking more antibiotics.

Dennis Lee, MD – authority in SIBO stated "However, antibiotics do have certain disadvantages. Specifically, symptoms tend to recur after treatment is discontinued, and prolonged or repeated courses of treatment may be necessary in some patients".[248]

According to Professor John K. DiBaise, M.D "The goal when treating SIBO should not be to sterilize the gastrointestinal tract but rather to reduce the numbers of pathogenic bacteria present".[163]

Small intestinal bacterial overgrowth (SIBO) is a relatively new condition and until now, it didn't have a "golden rule" for treatment.

It is the opinion of the authors, that SIBO is the advanced stage of dysbiosis when the opportunistic infections such as microbes, yeast, and parasites continue to grow and reside in the colon and small intestine.

The approach "*seek and destroy*" is not easy to accomplish in the case of SIBO. Multiple rounds of antibiotics kill the microbes. However, this can cause the development of their resistant strains. Certainly, antibiotics cannot easily destroy the yeast – the major part of dysbiosis. The

antibiotics just kill the friendly intestinal flora – the main guard against overgrowth of opportunistic infections.

Common sense and clinical evidences tells us that instead of focusing only on destroying the infections, it is necessary also to re-establish all possible mechanisms that naturally control the growth of opportunistic infections in the gut, which include strong stomach acidity, proper pancreatic function, normal bowel transit time, strong immunity, and restoration of the friendly intestinal flora. Some practical approaches will be found later in this book in chapter 39-*Whole Body Cleansing through the Restoration of Friendly Intestinal Flora and Colon Hydrotherapy,* and chapter 42-*Anti-Candida Program.*

m. The Harmful Effect of Dysbiosis on Exocrine Pancreatic Function and Digestion

In the holistic point of view, low exocrine pancreatic function and dysbiosis are in conjunction and become over dependent on each other. [162] Unhealthy diets full of processed products, red meat, sugars and unhealthy hydrogenate fats, as well as poor eating habits and stress are the main reasons for decreasing exocrine pancreatic function and the amount of friendly intestinal flora. These are the major causes of dysbiosis.

Italian researchers, Pezzilli R. *et al*. (2007), studied a possible link between pancreatic insufficiency and intestinal dysbiosis. The article, *Fecal calprotectin and elastase 1 determinations in patients with pancreatic diseases: a possible link between pancreatic insufficiency and intestinal inflammation*, was published in the *Journal of Gastroenterology* in 2007. [260] These researchers concluded that pancreatic insufficiency may cause intestinal inflammation, probably due to the modification of the intestinal ecology.

Many patients with GI complaints routinely get repeated courses of antibiotics either for *H.Pylori* eradication, or for other conditions such as stomach flu and food poisoning. The antibiotics can save the life after an attack of acute pancreatitis and they are the “golden rule” for treating this life threatening disease. It can be explained why there are almost no cases of patients with chronic pancreatitis without a history of using antibiotics.

Antibiotics can be present in many food products. For individuals with weak friendly intestinal flora and low immunity, even a small amount of antibiotics from meat, milk, chicken and fish can cause chaos in the “intestinal jungles”. In these cases, friendly intestinal flora is usually killed and opportunistic infections such as Candida-yeast take over the GI tract and cause dysbiosis.

Yeast fermentation produces very acidic substances. Typical examples of these acidic substances are alcohols, lactic acid, acetone and methanol (severe poison) along with the production of large quantities of the acid-forming gas carbon dioxide. Excessive absorption of toxins is derived from

the chemical activity of Candida- yeast, especially the acid-forming substances that stress the pancreas and liver.

All materials absorbed from the intestine must pass through the liver before entering the body's general circulation. The liver cells destroy or prepare the toxic chemicals to be excreted out of the body via the kidney or bile. The cost of detoxification is high; free radicals are generated and the liver storage of anti-oxidants is depleted. The products of detoxification may damage the liver itself. Damage may extend to the pancreas, as well. The acidic and toxic substances are excreted into bile; this "toxic" bile flows into the small intestine and can ascend into the ducts, which carry pancreatic juices and damage the pancreas, aggravating malnutrition.[42]

Sugar, wheat, yeast and warm water inside the bowels cause fermentation similar to the fermentation process in production of beer, vodka and other alcohols. This fermentation - "auto-brewery syndrome" poisons the body continuously and causes constant alcohol intoxication and severe damage to our alkaline glands (liver and pancreas). This leads to acidification of the bile and pancreatic juice. The acidic conditions promote manufacturing of the deconjugated bile acids, which are toxic to the colon walls and cause diarrhea. The deconjugated bile acids appear to be carcinogenic and are thought to contribute to the development of colon cancer and ulcerative colitis.[42]

Many digestive symptoms in dysbiosis result in a reduction in the absolute or functional intestinal absorptive surface area with development of the symptoms attributed to SIBO such as gas, bloating, abdominal cramping, diarrhea and steatorrhea. Fat maldigestion and malabsorption occur mainly due to the deconjugation of bile acids by intraluminal bacteria, allowing their absorption by the jejunum and leading to insufficient concentrations for micelle formation and fat absorption. Bacterial deconjugation may also result in the production of substances, such as lithocholic acid, which may exert toxic effects on the intestinal epithelium and result in impaired absorption of not only fat, but also carbohydrates and proteins. Because of the fat maldigestion and malabsorption that occurs in the setting of SIBO, deficiencies of the fat-soluble vitamins A, D, E and K can occur.

The main enemy for the pancreas - alcohol, is also harmful for friendly intestinal bacteria of the GI tract, as well. Alcohol is very toxic and feeds the yeast. Yeasts ferment sugar, producing additional alcohol and its by-products, acetaldehyde, n-propanol, lactic acid, hydrogen, acetone and even more exotic toxic substances that damage pancreatic cells.

In the overgrowth of intestinal Candida, the levels of alcohol entering the bloodstream are going to be greatly increased. In a study conducted by doctors at Biolab in London, UK, a number of chronically sick patients were tested for blood ethanol levels an hour after ingesting a sugar solution. The study found that patients consistently had high blood levels of ethanol, which the researchers concluded came from small intestinal yeast overgrowth.[159]

"Drunk disease" was first discovered in Japan when chronic candidiasis patients were tested and found to have alcohol in the blood even when they did not consume any alcohol at all. Japanese researchers also found that ethanol concentration even in blood samples taken after death continued to increase in people with candidiasis.[156]

The constant exposure to alcohol and acetaldehyde cause harmful effects on the body and particularly on the pancreas.

Some Harmful Effects of Dysbiosis on Pancreas Include:

> Constant production of very acidic components of alcohol metabolism causing chronic metabolic acidosis. Acidity kills the pancreas

> Degeneration of the pancreas with the reduced ability to produce pancreatic enzymes, which impair digestion and alter the metabolism of proteins, carbohydrates and lipids in the body

> Nutritional deficiencies from damaging effects on digestion and absorption of most vitamins, minerals, trace elements and amino acids. Deficiencies in A, D, E, K and B vitamins are particularly common

> Liver damage with the reduced ability to detoxify drugs, toxins, and other chemicals and dispose of hormones and other byproducts of normal metabolism

> Reduced ability of the stomach wall to produce stomach acid

> Damage to the immune system

> Brain damage, which can have a negative impact on the pancreatic regulation and function, manifesting with lack of self-control, cravings, anxiety, depression, aggression, and peripheral nerve damage

n. Dysbiosis triggers low exocrine pancreatic function

Gastrointestinal disorders are the complex component of interrelated “vicious circles”. Here is an important example:

Low exocrine pancreatic function => =>dysbiosis => =>low exocrine pancreatic function

Now we will focus on the mechanisms on how dysbiosis, Candida-yeast overgrowth and SIBO negatively influence the exocrine pancreatic function.

i. Link Between Dysbiosis, the Decreased Activity of Pancreatic Digestive Enzymes Inside the Small Intestine and Subsequent Indigestion

During the past 30 years, an increasing number of reports began to be published about injuries to the guts' cells by intestinal bacterial toxins. A major consequence of dysbiosis relates to the inflammatory epithelial changes that subsequently occur in the gut.

Unfriendly intestinal flora destroys pancreatic digestive enzymes, as well. Failure to digest food because of insufficient gastric acid, lactase, or other digestive enzymes, allows more nutrients to reach the lower small intestine and colon, where the microflora can then overgrow.

Len Saputo, M.D. stated in his article *Dysbiosis and Irritable Bowel Syndrome (IBS),* "This bacterial overgrowth can lead to the overproduction of enzymes (proteases) that are able to degrade enzymes produced by the intestinal lining and the pancreas, and can result in maldigestion. This type of dysbiosis has been called "fermentation excess dysbiosis".[140]

ii. Deficiency of the Vital Nutrients in Dysbiosis

Insufficient activity of the digestive pancreatic enzymes, the presence of toxic bile and decreased absorption in the gut lead to maldigestion and also to many deficiencies of the fat-soluble vitamins (A, D, E, and K). Overgrowth of the opportunistic infections competes for nutrients with the host that aggravates the deficiency of essential nutrients. Vitamin B12 deficiency is caused by bacterial consumption involving predominantly anaerobic organisms within the intestinal lumen before this vitamin can be absorbed. Deficiencies of thiamine and nicotinamide have also been reported.[163] A lack of nutrients badly influences the normal function of the pancreas, as well.

iii. Dysbiosis and Body Acidification

Acidity decreases the activity of pancreatic protease – the primary enzyme that digests the protein and the harmful parasites, microbes and fungi (yeast), as well. In turn, it causes Small Intestinal Bacterial Overgrowth (SIBO). This involves overgrowth of bacteria in the small intestine rather than the colon. The result is the same type of problem as with yeast overgrowth (also predominantly in the small intestine) whereby the sufferer develops an intolerance to carbohydrates.

Any ingested carbohydrates are fermented by bacteria and result in production of toxic waste products such as organic acids (acetic acid, lactic acid) and hydrogen sulphide (H2S), all of which are potentially toxic in increased amounts and can lead to metabolic acidosis. Acidity kills the pancreas and diminishes activity of pancreatic enzymes, thus, causing indigestion and malnutrition.

Too many acidic radicals can lead to a "vicious circle" such as

Chronic metabolic acidosis => Low exocrine pancreatic function => Low anti bacterial activity of pancreatic enzymes and bile => Dysbiosis => Chronic metabolic acidosis

iv. Candida, Alcohol and Acetaldehyde - Toxic Substances for Pancreatic Cells

Constant intestinal fermentation produces a large number of the toxic acidic byproducts. They can cause damage to the acinar pancreatic cells and activate digestive pancreatic enzymes inside the pancreas that can lead to possible chronic pancreatitis and low exocrine pancreatic function.

v. Candida and Chronic Pancreatic Inflammation

Our immune system can malfunction by at least three ways: weakness, overreaction and improper function.
Being overwhelmed with invaders such as unfriendly intestinal flora, Candida-yeast or other chronic infections can weaken the immune system. Some viruses, chemotherapy agents, cancer, and even stress also trigger the weak immune system. Caused by Candida-yeast overgrowth, indigestion, maldigestion and subsequent deficiencies of many vital nutrients lead to the exhaustion of the immune system so that it cannot make an adequate response. This is referred to as immune suppression and often occurs at the final stage of chronic pancreatitis – *pancreatic failure.*
The immune system can overreact in a way where it becomes hyper-responsive to normal stimuli. This situation often occurs in the leaky gut syndrome when the Candida-yeast overgrowth increases permeability of intestinal wall mucous membranes, allowing the large particles of improperly digested food to penetrate into the blood. The immune system becomes over-reactive. Examples of the immune system over-reacting include asthma, migraines or food allergies. Food sensitivities, food intolerance and food allergies are very common in most digestive (pancreatic) disorders. This can result in not only using up the immune reserves of the body, but may cause immune reactions that create tissue injuries in the GI tract, including the pancreatic gland.

After overreacting, the immune system can start to work improperly, thus, causing auto aggression - autoimmune reactions, wherein antibodies are made against the host's own tissues. Examples of the immune system improperly working include rheumatoid arthritis, Crohn's Disease, Hashimoto thyreoiditis, lupus, or autoimmune pancreatitis.

Regardless of the mechanism of immune system malfunction, the final result is the same; the abnormal host defense mechanisms can lead to the next vicious circle as

Immune system malfunction => pancreatitis => antibiotics => dysbiosis => immune system malfunction

vi. Candida and Pancreatitis

Infections of the pancreas by Candida-yeast were considered extremely unusual for many years. Now, these infections are being recognized as important, albeit infrequent, problems. The web site: http://www.doctorfungus.org/mycoses/human/candida/Pancreatitis.php has an interesting article with many references about pancreatic candidiasis. Candida infection may occur either as part of a mixed infection or by itself. Some researchers reported rates of pancreatic candidiasis at 41%.[166]

Patients with pancreatitis are frequently exposed to several risk factors for invasive candidiasis, including:

1. Use of multiple & broad spectrum antibiotics
2. Central venous lines
3. Multiple deep abdominal surgeries (recent pancreatic surgery has been specifically associated with pancreatic candidiasis)
4. Total parenteral nutrition

Both endoscopic retrograde cholangiopancreatography (ERCP) and pancreatic transplants have been associated with Candida infection of the pancreas.
http://www.doctorfungus.org/mycoses/human/candida/Pancreatitis.php

o. Diminished Exocrine Pancreatic Function and the Aggravation of Dysbiosis

There are many ways that "vicious circles" and numerous "endless loops" display the mechanism of developing dysbiosis (Candida-yeast overgrowth and SIBO) if the exocrine pancreatic function is decreased. The major mechanisms are:

i. Decreasing the antibacterial activity of pancreatic enzymes

ii. Low activity of digestive pancreatic enzymes leading to fermentation and putrification in the small intestine

iii. Low exocrine pancreatic function propitiating harmful changing of bile biochemistry

iv. Low pancreatic enzymes and bile triggering gut motility and causing constipation

v. Intestinal dysbiosis having a direct connection to exocrine pancreatic deficiency disorder

***i.* Decreasing the Antibacterial Activity of Pancreatic Enzymes**

The pancreatic juice plays a very crucial role in bacterial homeostasis in the gastrointestinal tract, especially in the duodenum. There are indications of the existence of a relationship between the altering of intestinal micro flora and pancreatic function. Normally, pancreatic juice has very strong antimicrobial activity. It protects the pancreas and biliary tree against ascending infections and preserves bacterial homeostasis in the small intestine. Pancreatic juice is active against a whole spectrum of microorganisms. The antibacterial action of the pancreatic juice appears to be

very sensitive to pH, having an optimal activity pH of 8.5 and with complete action cessation pH of 7.0.[148,149]

This can result in a possible vicious circle such as:

Antibiotics => Candida-yeast overgrowth => increasing acidity => cessation of antibacterial activity of pancreatic juice => dysbiosis => pancreatitis => antibiotics

Dysbiosis may complicate the course of both acute and chronic pancreatitis and may be particularly prevalent, with reports of up to 40% in those with associated pancreatic exocrine insufficiency.[162,163,164,165, 175]

The viscous circle is likely with multiple factors including disease-related and treatment-related conditions such as opioid analgesics, NSAID, intestinal dysmotility, lower stomach acid, alterations in secretions of pancreatic juice and bile, etc.

In the worst case scenario, pancreatic juice loses its antibacterial activity and this can lead to SIBO - Small Intestine Bacterial Overgrowth. SIBO is a disorder of excessive bacterial growth in the small intestine. Unlike the colon (or large intestine), which is rich with bacteria, the small bowel usually has less than 104 organisms per milliliter. In a healthy subject, the main mechanisms restricting the bacterial colonization in the upper gut (duodenum) are the:

1. Gastric acid barrier
2. Antibacterial activity of pancreatic juice and bile
3. Mucosal and systemic immunity
4. Intestinal clearance [163]

When these mechanisms fail, bacterial overgrowth develops. Failure of the gastric acid barrier can be caused by *Helicobacter pylori*-induced gastritis, drug-induced inhibition of acid secretion, autoimmune diseases, malnutrition, and aging. Regarding local mucosal and systemic immunity, conditions such as HIV or immunoglobulin deficiencies (IgA deficit) can be linked to SIBO development. Failure of intestinal clearance can be associated with anatomical abnormalities, such as gastrointestinal surgery, intestinal diverticula or fistula and conditions that impair intestinal peristalsis such as myopathic, neuropathic, autoimmune, inflammatory, metabolic, and endocrine diseases.[157] Dehydration and constipation also may diminish intestinal clearance.

Thanks to the development of SIBO diagnostic tests such as breath tests, D-*xylose* urine and blood tests, *quantitative culture of intestinal fluid aspirate*, biopsies of the small bowel, etc., doctors are more aware of intestinal dysbiosis. Because of the advancement of this technology, this condition has recently started capturing the attention of researchers, doctors and other specialists. Let’s focus on the role of antimicrobial activity of pancreatic juice and bile in development of the SIBO and what kind of factors can diminish or improve this one.

The regulation of intestinal microbial homeostasis is a multifactor phenomenon and pancreatic juice plays a very important role. There are indications of the existence of a relationship between the altering of intestinal microflora and pancreatic function. The microflora defends the pancreas and biliary tree against ascending infections and maintains bacterial homeostasis in the small intestine.[148]

On the other hand, low antibacterial activity of pancreatic juice and bile can lead to pancreatitis and/or SIBO. Rubinstein *et al*. [149] have shown that the antibacterial activity of pancreatic juice is highly sensitive to changes in pH and change from an alkaline condition to a neutral condition will completely cease the antibacterial activity.

Apparently the only thing that antibacterial factor is sensitive to is pH, suggesting that the alkaline nature of the exocrine pancreatic secretion, brought about by a high concentration of bicarbonate ions, is not only meant for neutralization of the gastric acid. [148] It has been discovered that in patients with pancreatitis there is a significant drop in the pH of pancreatic juice, which may pave the way for bacterial invasion since the action of the inherent antimicrobial factor is lost.[148, 158,175] The bicarbonate is a key ingredient, which makes the pancreatic juice alkaline. A connection between the decreasing of bicarbonate output and low exocrine pancreatic function is an established fact by many authors.[101,102, 113, 116, 175]

All kind of "crash diets", harsh "liver cleansing", fasting, and starvation cleansing techniques may aggravate dysbiosis by diminishing antimicrobial activity of the pancreatic juice.

In an experiment, starvation of 48 hours caused a drop in the rate of secretion as well as in the antibacterial potency of the pancreatic juice. It is very likely that during starvation, the system of information exchange between the upper small bowel (duodenum) and pancreas fails to be activated and that this results in a weak antibacterial response in the pancreatic juice. This hypothetical system postulated by Pierzynowsky *et al.* may be a crucial one that signals to the pancreas when to produce more or less of the antibacterial factor.[148, 158]

It is the opinion of the authors that the loss of pancreatic juice and bile antibacterial activities are the main triggers of SIBO. Eradication of bacteria in the small intestine by repeated courses of strong antibiotics without restoration of antibacterial activity of pancreatic juice may have a temporal effect. In this scenario, we only "win the battle, but lose the war".

In the long run, the situation is aggravated by the eradication of friendly intestinal flora, thus causing dysbiosis.

ii. Low Activity of Digestive Pancreatic Enzymes Leading to Fermentation and Putrification in the Small Intestine

In healthy conditions, food is properly digested, and absorbed in the small intestine. Contrary, indigested and non-absorbed food feed the uninvited guests such as bacteria, yeast and parasites, thus, making an excellent environment for them to thrive. Proper digestion depends on proper

exocrine function of the pancreas, which means there is the right amount and good quality of pancreatic digestive enzymes and bile.

iii. Diminished Exocrine Function of Pancreas May Promote Dysbiosis, SIBO and/or Candida- yeast Overgrowth

It is easy to explain the worsening of conditions of people with chronic pancreatitis after meals. Immediately after eating, these individuals feel bloating, gas, pain, abdominal cramps and fullness. At that time, unfriendly bacteria and yeast multiply and produce the toxins and gas (hydrogen, carbon dioxide, methane) that may be responsible for a variety of symptoms such as "gas," bloating, distension, and abdominal discomfort.

Noninvasive breath tests, especially the Glucose Breath Test (GBT), are widely used to diagnose Small Intestine Bacterial Overgrowth. Breath testing is now the predominant method to evaluate patients for potential overgrowth because of its simplicity, safety, and lack of invasiveness. These tests analyze production of gases, which are generated by intestinal bacteria and are exhaled after ingestion of a fermentable carbohydrate like glucose or lactulose.

The most common detectable gases are hydrogen and methane, which are indicators of bacterial metabolism in the gut. Many researchers found the *Glucose Breath Test* to be positive in patients with IBS.[160, 161] The results of those tests varied, but 30%-50% is very substantial to ignore the connection of IBS and dysbiosis, particularly SIBO. 66% produced only hydrogen, 29% produced only methane and 5% produced both hydrogen and methane. There were more methane producers in the IBS-Constipation group then the IBS-Diarrhea group (58% vs. 28%) while the IBS-Diarrhea group had more hydrogen formers (71% vs. 42%). Results showed that in the IBS-Diarrhea group, hydrogen production was greater than methane, thus more susceptible to Candida –yeast overgrowth. Yeast usually ferments sugars with a production of large amounts of hydrogen.

iv. Lower Exocrine Pancreatic Function Goes Together with Harmful Changing of Bile Biochemistry

Manibusan PA *et al.* (2009) [162] underlined that "malabsorption of bile acids, fats, carbohydrates, proteins, and vitamins results in direct damage to the lining of the luminal surface by bacteria or by transformation of nutrients into toxic metabolites, leading to many of the symptoms of diarrhea and weight loss associated with bacterial overgrowth syndrome." This leads to decreased function of the enterocytes within the intestinal lining and subsequent malabsorption. Unabsorbed food products stimulating secretory cells within the colon propitiate diarrhea.

Some anaerobic bacteria actively deconjugate bile acids, thereby preventing proper bile acid function and enterohepatic circulation:

> Fatty acid absorption is reduced because deconjugated bile acids cannot form micelles

> Deconjugated bile acids directly inhibit carbohydrate transporters. These unabsorbed sugars ferment into organic acids, thereby reducing the intraluminal pH and producing osmotic diarrhea. The deconjugated bile acids also damage intestinal enterocytes and induce water secretion by the colonic mucosa

> Loss of bile acids in the stool reduces the "bile acid pool"[162]

Wide ranges of bile salt malabsorption were observed in patients with exocrine pancreatic insufficiency. The fecal loss of bile salts in patients was markedly reduced by oral administration of pancreatic enzymes, indicating an important role for pancreatic enzymes in bile acid absorption.

Raffaele Pezzilli, MD, suggested that "bacterial overgrowth might give rise to bile acid malabsorption and changes in intestinal permeability. Low intraluminal pH in the upper small intestine might be another important factor in the pathogenesis of fecal loss of bile acids in pancreatic insufficiency. Thus, bile acid malabsorption in patients with chronic pancreatitis and exocrine dysfunction does not occur until bicarbonate output is below a certain level".[175]

It can be postulated that deconjugated bile acids can irritate the ileocecal valve. This can cause the ileocecal valve to function improperly, thus, allowing bacteria and yeasts from the colon to use this pathway to reach the small intestine. Along with low pancreatic juice antibacterial activity, low exocrine pancreatic function can make a terrain for parasites and yeast to thrive, especially in the bile ducts, causing bile stagnation, as well.

v. Low Pancreatic Enzymes and Bile Trigger Gut Motility Causing Constipation

Insufficient levels of hydrochloric acid in the stomach, or pancreatic digestive enzymes and bile salts are the most essential factors for developing dysbiosis. All these factors can decrease intestinal propulsive activity and lead to constipation. Intestinal motility represents one of the major control systems of gut microflora by sweeping excessive bacteria from the lumen. Normal small bowel motility is the first defense against the attachment of bacterial organisms to intestinal walls. On the other hand, constipation is the important symptom of deficiency of friendly intestinal flora, which results in dysbiosis.

p. Intestinal Dysbiosis Having a Direct Connection with Exocrine Pancreatic Deficiency Disorders

Like all chronic diseases, dysbiosis has also three stages: functional, partially reversible with structural damages and the decompensating final stage. For methodology purposes, dysbiosis can be divided conditionally into broad categories based upon severity.

In Candida-yeast overgrowth the process primarily involves the large intestine (*acidic pancreas and bile* stage), Then, Small Intestine Bacterial Overgrowth (*pancreatic deficiency* stage) occurs, when the opportunistic infections, including Candida-yeast inhabit the small intestine. Finally, when the microorganisms leave the GI tract, and go into the blood and occupy the entire body, Candidemia (*pancreatic failure* stage) develops.

Taking in account that dysbiosis and pancreatic exocrine function are deeply interrelated and have many similar symptoms, it can be practical to use the *Biotherapy Functional Clinical Classification of Exocrine Pancreatic Disorders* to evaluate different stages of dysbiosis. See chapter 7.

Intestinal dysbiosis <===>Exocrine pancreatic deficiency disorders

Acidic pancreas and bile stage associates with the functional stage of dysbiosis. There are so far no structural damages; as a result, there are minimal changes in the tests and relatively mild clinical symptoms. Candida, unfriendly intestinal flora, parasites reside just in the large intestine.

Possible diseases and conditions associated with this stage include functional dyspepsia, IBS, Sphincter of Oddi Dysfunction type III, and constipation.

During *pancreatic deficiency* stage, some structural damages in the gut aggravate symptoms of intestinal dysbiosis, and combine with possible pancreatic damage. Symptoms, especially pain and indigestion, are steady with a tendency to exacerbate, but can be reversed to stable remission.

The Comprehensive Stool Analysis with Parasitology test reveals the beginning of maldigestion and the pathological ratio between friendly and unfriendly intestinal flora and growth of *Candida albicans.* Breath tests can also confirm the SIBO.

Possible diseases and conditions associated with this stage include attacks of acute pancreatitis (some of them maybe very mild), chronic pancreatitis, Small Intestine Bacterial Overgrowth (SIBO), chronic Candidiasis, Sphincter of Oddi Dysfunction type I or II, gallbladder disorders (inflammation, stones, sludge, parasites), conditions after gallbladder removal and some surgeries on the upper GI tract, IBD (Crohn's Disease, Ulcerative Colitis) and Celiac Diseases.

Symptoms of dysbiosis in the stage of *pancreatic failure* include constant abdominal pain, maldigestion and malabsorption, steatorrhea (smelly stools containing oil) and weight loss. Dysbiosis, as systemic candidiasis, regularly accompanies this stage and without proper action leads to serious consequences. Diagnosis of chronic pancreatitis and dysbiosis in this stage can more or less be verified by conventional tests. Possible diseases and conditions associated with *pancreatic failure* include the final stage of chronic pancreatitis, liver cirrhosis, cancer and invasive candidiasis.

Pancreas disorders and dysbiosis are interrelated and usually aggravate each other. All preventive and treatment options for these conditions have to be done simultaneously.

"Friendly" intestinal flora plays an important role in our ability to fight infectious disease, providing a front line in our immune defense, giving a passive mechanism to prevent infections and producing many vitamins and vital nutrients.

Interesting facts at a glance:

For the last 50 years, the world has faced a pandemic of interrelated conditions: digestive disorders, metabolic acidosis and dysbiosis

Millions of Americans suffer from dysbiosis (Candida-yeast overgrowth or Small Intestine Bacteria Overgrowth)

Approximately every third woman in the United States has a history of vaginal yeast infection, yet does not realize that it is a symptom of Candida-yeast overgrowth in the whole body

The gastrointestinal tract is home to more than 400 species of microorganisms. They can be beneficial, harmful or opportunistic

The term "probiotic" is used to describe beneficial (friendly) bacteria that are essential "for life." Friendly intestinal flora is vital for the human organism

Without healthy friendly intestinal flora, we cannot expect robust health and overall well-being

Friendly intestinal flora performs many functions, including controlling the growth of opportunistic infections

Modern food and lifestyles, using antibiotics, hormones and stress have a negative impact on the friendly intestinal flora

A low amount of friendly intestinal flora creates an opportunity for opportunistic infections to grow. This condition is called Intestinal Dysbiosis

Intestinal Dysbiosis can result from a deficiency of good bacteria losing their health benefits. In addition, Intestinal Dysbiosis is an overgrowth of harmful organisms such as Candida-yeast, parasites or other harmful bacteria in the small and large intestines

Candida-yeast is the most frequent opportunistic infection, because antibiotics cannot destroy yeast

When opportunistic infections multiply, Candida-yeast produces a large number of toxic and acidic substances that lead to disorders of the nervous, immune, hormonal, muscular and, certainly, the digestive system

Hidden or obvious dysbiosis can trigger a great number of disorders and diseases, which can be seen now in epidemic proportions

Candida-yeast promotes the growth of other opportunistic infections that begin to occupy the small intestine causing Small Intestine Bacterial Overgrowth

Intestinal dysbiosis <=> Exocrine Pancreatic Deficiency Disorders

Low exocrine pancreatic function promotes dysbiosis and candidiasis

Low antibacterial activity of the pancreatic juice leads to dysbiosis

Low activity of digestive pancreatic enzymes leads to fermentation and putrefaction in the small intestine

In most cases, low exocrine pancreatic function goes in conjunction with a harmful change of the biochemistry of bile. This change causes the precipitation of the bile acids, which irritate the GI tract

Low pancreatic enzymes and bile trigger motility and cause constipation. Constipation is a milieu for opportunistic infections to multiply

Dysbiosis, candidiasis and SIBO promote low exocrine pancreatic function

Dysbiosis decreases the antibacterial activity of pancreatic enzymes

Dysbiosis decreases the activity of pancreatic digestive enzymes inside the small intestine

Both dysbiosis and Candida - yeast overgrowth acidify the body causing metabolic acidosis

Candida-yeast produces alcohol and acetaldehyde, both of which are toxic substances for pancreatic cells

Candida-yeast can cause a malfunction of the immune system, leading to chronic pancreatitis

Candida-yeast may directly cause pancreatitis

Low pancreatic function and dysbiosis are interrelated and usually aggravate one another

All preventive and treatment options for these conditions must be done simultaneously

The "eradication" of dysbiosis through the use of strong antimicrobial or antifungal agents has no effect on causation, and therefore, only supplies temporary results Elimination of the causation generally leads to the elimination of dysbiosis

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Chapter 16-The Role of Exocrine Pancreatic Deficiency in Metabolic Syndrome, Obesity and Diabetes

For individuals lacking a medical background

The pancreas is a unique organ with many talents and tasks. Essentially, it is our cellular manufacturing plant with complete equipment to promote healthy digestion and sugar processing. Pancreatic cells produce a variety of digestive enzymes (trypsin, chymotrypsin, lipase, and amylase, among others) and bicarbonates that travel into the small intestine and hormones (such as insulin) that are released into the blood.

a. Pancreatic Functions and Diseases

Traditionally, those two functions of the pancreas are divided. For example, pancreatitis is the responsibility of gastroenterologists, but diabetes is the responsibility of endocrinologists with frequently different points of view on prevention and treatments.

These two digestive and hormonal pancreatic functions interrelate and in many situations, have the same reason for malfunctioning.
For example, pancreatitis causes the development of diabetes. Diabetes, in its turn, diminishes production and activity of digestive pancreatic enzymes.

It is shown that pancreatic deficiency is very common in diabetic patients (32% - 50%). Some individuals with diabetes are actually suffering from chronic pancreatitis but symptoms of pancreatic deficiencies are not specific in the early stages of chronic pancreatitis and it is difficult to diagnose in everyday practice.

On the other hand, the prevalence of diabetes mellitus in chronic pancreatitis is 40-70%. Chronic pancreatitis and diabetes are commonly overlapping conditions.

Pathological conditions in the exocrine tissue can cause impairment of endocrine function and vice versa

All parts of the pancreas have a blood supply and nervous regulation. All functions of the pancreas (digestive and hormonal) are dependent on each other and are affected by nervous regulation, diets, lifestyles, and toxic environments inside and outside the pancreas. Diseases of the pancreas such as inflammation, infections, parasites, tumors, and hereditary and metabolic disorders negatively influence both digestive and hormonal functions.

For the past 30 years, medical statistics alertly show an increase in epidemic proportions of both “diabesity” (diabetes + obesity) and digestive diseases all over the globe. No question, both digestive and metabolic disorders have a strong relationship with the pancreas and its function.

With the aging population of the United States, the mixed incidences of obesity, Metabolic Syndrome, diabetes, many digestive disorders, IBS, dysbiosis and a host of other similar diseases have been steadily rising, reaching epidemic proportions.

b. Metabolic Acidosis, Metabolic Syndrome and Syndrome X

The authors suggest factors that negatively influence either the digestive or hormonal functions of the pancreas. The main factor is whole body acidity, which is referred to as chronic metabolic acidosis.

Guess what is more dangerous for the American population: a terrorist attack, an infection epidemic, environmental hazards or an alien invasion? Well, none of the above. According to recent data, health conditions such as heart disease, stroke, diabetes, cancer and other health killers will take the lives of almost 70 million Americans in the future. You may already be suffering from one of the most common and often overlooked diseases to strike Americans. Doctors call this peculiar condition insulin resistance or, with a bit more mystique, Syndrome X or Metabolic Syndrome.

This peculiar disease is responsible for the deaths of 2,600 Americans daily. Every 33 seconds it claims another victim! That is because of stress, lack of physical activity, drinking alcohol, environmental pollutants, aggressive toxic chemicals, and a diet high in processed, acid-producing foods collectively create the underlying cause of the worst enemy of the pancreas; metabolic acidosis. Acidity literally kills the pancreas, paving the way for pancreatic diseases to take over.

Millions of Americans suffer from indigestion, heartburn, abdominal cramps, gas, bloating, loose stool or constipation because acidity diminishes the exocrine (digestive) function of their pancreas. Chronic metabolic acidosis (body acidity) has a primary relationship with the development of the following conditions: being overweight, obesity, Metabolic Syndrome, belly fat, fatty liver, fatty pancreas, and diabetes.

Why are individuals with metabolic acidosis prone to gaining weight with fat deposit? Let's explain it. 30,000 years ago, our "hunter-gatherer" ancestors did not have readily available access to supermarkets or refrigerators. They had times of abundant food supply, but unfortunately, more frequent periods of famine. That is why most individuals have a special genetic mechanism that gives them the opportunity to survive in periods of starvation. This is referred to as the starvation mode of metabolism. Simply, metabolism becomes very low and economical.

Because individuals do not have a large reserve of carbohydrates, their bodies' use their own fat and muscle protein during starvation. This process usually is accompanied by releasing lots of acidic substances (ketones, diacetic acid, lactic acid). This process depletes the blood of its alkaline reserve and leads to whole body acidity.

Too much acidity signals to the body that the organism has to be very economical and must be changed into the starvation mode of metabolism. Then, everything eaten, especially carbohydrates go into fat storage to be collected for a "rainy day" as a reserve. Collected body fat is the main inner source of carbohydrates during starvation.

Despite overeating, the body can be acidic by acid-producing foods. Acidity causes the carbohydrate metabolism to be low, resulting in the body gaining weight. This leads to more obesity.

c. Chronic Metabolic Acidosis, Insulin and Diet

Chronic metabolic acidosis is the main factor of insulin resistance – the condition when the cells shut down for actions of the pancreatic hormone insulin. The pancreas produces more and more

insulin and, if it is not used, the insulin collects in the blood. At high levels, insulin is harmful for the body. In Metabolic Syndrome (also called insulin resistance syndrome), plasma insulin concentration is higher than normal. It is a syndrome of impaired carbohydrate, fat, and protein metabolism caused by decreased sensitivity of the tissues to insulin.

Our body uses insulin as a storage hormone. When the body is exposed to high levels of sugar, pancreatic insulin secretion insures storing excess sugars as fats in case of future famine. Insulin can convert almost half of your dietary carbohydrates into fat for storage. When we eat too many carbohydrates, we are sending a hormonal message, via insulin, to the body to "store fat" and not release any currently stored fat.

People have evolved for thousands of years on the "caveman diet" of meat, fish, vegetables and fruits. When modern civilization began about 10,000 years ago, our physiology suddenly was asked to digest and metabolize larger amounts of sugars and starches (especially nowadays - refined sugars). Sugars are very acidic. They deplete our alkaline reserve capacity of minerals and bicarbonate causing whole body acidity – metabolic acidosis.

Researchers found that our ancestors had plenty of minerals such as potassium, magnesium, calcium and bicarbonates from their food and in case of acidosis they easily neutralized too much acidity in the body. Unfortunately, this does not occur nowadays. Scientists from the Department of Medicine and the General Clinical Research Center, University of California, San Francisco, Lynda Frassetto, R. Curtis Morris Jr., Karen Todd and Anthony Sebastian found that normal adult humans eating modern-day diets have a chronic low-grade metabolic acidosis whose severity is determined in part by the net rate of acid production.[49]

No wonder, that a diet high in acid-producing foods such as sugar, white flour, sweets, alcohol, bad fats and red meat results in severe chronic metabolic acidosis, insulin resistance and finally Metabolic Syndrome. This depletes the blood of its alkaline reserve and the body tries to remove the access of acid radicals through the body fluids such as saliva and urine. By using a very simple litmus paper test at home everybody can check his or her saliva and urine pH. This is a window inside the body's acid-alkaline balance.

We have to focus more on Metabolic Syndrome as a beginning stage of many metabolic and digestive problems connected to the pancreatic health. Metabolic Syndrome, also known as Syndrome X, is the combination of obesity, high cholesterol, and hypertension linked by an underlying resistance to insulin. This condition is often associated with excess insulin secretion.

In 1998, American endocrinologist and professor of medicine from Stanford University, Dr. Gerald Reaven, first described this syndrome.

Retrospective data from the National Health Nutritional Survey for the period 1988 to 1994 implied that 47 million Americans had Metabolic Syndrome. The current prevalence of the syndrome may now be one in every four adults in the United States population, or about 70

million individuals. So common and pernicious are the negative health outcomes of Metabolic Syndrome that it qualifies by Stephen Holt, MD, in his article, *Obesity, Prediabetes and Metabolic Syndrome X,* as the number-one public health problem facing several Western societies.[334]

The number of people with Metabolic Syndrome increases with age, affecting more than 40 percent of people in their 60s and 70s. The development of Metabolic Syndrome begins from a diet full of the simple carbohydrates such as sugar and white flour. Easy digested sugars increase the level of glucose in the blood that pushes the pancreas to produce more insulin to move the glucose into the cells for energy.

However, cells do not need too much glucose and become resistant to insulin. More glucose in the blood forces the pancreas to manufacture more insulin. When the cells are more resistant to insulin there are high levels of insulin and glucose in the blood that can be seen in adult onset diabetes.

M. Murray, ND considers that, pre-diabetes, Syndrome X is a serious disease because it is a sign of serious disruption of physiological processes. Think of it as a sign of the body in **chaos**.

Coronary artery disease, **H**ypertension, **A**dult onset diabetes, **O**besity, **S**troke

In fact, “chaos” is a good acronym by Dr. Murray for the various complications of Syndrome X. Syndrome X carries a huge risk of suffering from these potentially catastrophic health conditions. Although the Metabolic Syndrome is identified as a major cause of cardiovascular disease and diabetes, it increases deaths and disabilities from all causes, and underlies digestive problems, reproductive disorders, female polycystic ovary syndrome, fatty liver disease, gout, memory disorders, and certain cancers.

If the name “Metabolic Syndrome” does not sound familiar, the symptoms probably will:

> Feeling tired after eating and at other times when one should not

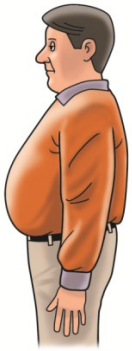
> Gaining pounds around the belly and having difficulty losing them

> Slow increasing of blood pressure and cholesterol

> Craving sweets, breads or other carbohydrates shortly after eating

> Suffering from "brain fog"

Hundreds of studies have led to the conclusion that any excess of fat in the body can be problematic, but it is much, much more dangerous when it is accumulated in the abdomen, making it "apple shaped.” http://www.aafp.org/afp/20010315/1165ph.html



To find out whether you have an apple figure, determine your **waist-to-hip ratio**:

1. Take your waist measurement with a tape measure around your waist in the level of your navel

2. Then take your hip measurement by measuring your hips at their widest point

3. Determine your waist-to-hip ratio by dividing your waist measurement by your hip measurement

An unhealthy accumulation of fat in the middle, or an apple figure, suggests for women a ratio over 0.8 and for men a ratio over 1.0 as hallmarks of Metabolic Syndrome.

People who store fat primarily in their bellies are at high risk for heart attacks and diabetes. After you eat, blood sugar levels rise. If they rise too high, they call out huge amounts of insulin. The cells become resistant to high levels of insulin in what is called “insulin resistance”. Insulin loses its ability to make your body's cells absorb glucose from the blood. When this happens, glucose and insulin levels remain high after you eat. High levels of insulin in the blood can cause blood vessels spasms, thus high blood pressure, damaging of blood vessels, and an increased propensity for heart attacks, strokes, diabetes, asthma, dementia, infertility, and even cancer.

The liver suffers from Metabolic Syndrome too. Fatty liver is a typical part of Syndrome X or Insulin Resistance Syndrome and one of the most common and often overlooked conditions. It is a very important to have proper liver function to remove insulin from the bloodstream. Belly fat shows fat storage in the liver, as well. Fat deposits break the liver functions and prevent the liver from removing insulin. As a result, insulin levels rise higher and higher and cause damage inside the lining of blood vessels. Consequently, this leads to spasms, hypertension, heart attacks, stroke, cancer, abdominal obesity and eventually diabetes.

Excess of insulin acts as a toxin for the rest of the body

When insulin resistance occurs, glucose levels remain high after eating. The pancreas, sensing a high glucose level in the blood, continues to excrete insulin. It closes arteries to cause heart attacks, spasms the vessels to rouse strokes, and acts on the brain to make one eat more. In addition, the insulin acts on the liver to manufacture more fat and for that fat to be stored in the belly.

Fat that is collected inside the abdomen can also be transferred to the liver and pancreas. Fatty pancreas is a condition when the fat is deposited inside the pancreatic gland. This diminishes pancreatic function.

Why Are Metabolic Syndrome and Diabetes Rates Growing and Threatening to Become the Diseases of the Civilization?

The authors have three big reasons to explain this: poor nutrition, sedentary lifestyle, and stress.

1. Poor Nutrition. Many Americans are literally eating themselves to an early death. Today, researchers recognize that Metabolic Syndrome is a nutritional disease caused by overconsumption of white flour, sugar and other products with a high glycemic index and also animal fats, alcohol. On the other hand, this condition is caused by a deficiency of vital nutrients such as vitamins, minerals, microelements, fibers and essential fatty acids in our food. Body acidity, which is caused by the Standard American Diet, obviously decreases the sensitivity of cells to insulin. A rise in the blood glucose levels causes an immediate release of insulin, presumably that is stored in the beta-cell granules of the pancreas.

2. Sedentary Lifestyle. Without enough movement the muscle cells do not need glucose for energy and become insulin resistant. Regular exercise is vitally necessary to keep the insulin in balance and to improve glucose and triglyceride levels.

3. Chronic Stress. Elevated levels of the cortisol stress hormone will increase appetite, enhance fat storage, disrupt blood sugar control and eventually lead to obesity that can cause Metabolic Syndrome and other serious conditions such as diabetes. Stress leads to increased cortisol secretion and can produce elevated levels of sugar in the blood (hyperglycemia). A rise in the blood glucose levels causes an immediate release of insulin that is stored in the beta-cell granules of the pancreas. This causes insulin resistance, which means that once the insulin starts "giving orders" to dispatch the blood glucose, the body does not pay attention. The insulin is rendered ineffective, and the carbohydrates are not metabolized properly.

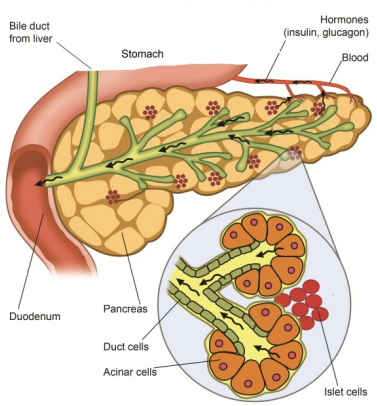
Repeated insulin release to lower sugar in the blood eventually can lead to insulin resistance. The beginning of this process leads to episodes of hypoglycemia (attacks of hunger) and then to hyperglycemia (diabetes). High insulin levels are the cause of Metabolic Syndrome, which is directly implicated in obesity, type 2 diabetes, atherosclerosis, high blood pressure, heart disease, fatty liver and pancreas, periodontal diseases, polycystic ovarian syndrome, cancer and pancreatic disorders.

For individuals with a medical background

d. Anatomical and Functional Links between the Exocrine and Endocrine Pancreas

In consequence of the close anatomical and functional links between the exocrine and endocrine pancreas, any disease affecting one of these parts will inevitably affect the other.

On an anatomical level, the endocrine and exocrine systems have deep interrelationships. Special pancreatic cells do unique jobs. Insulin-secreting cells associated with the enzymes and the bicarbonate produced ductal system count for 15% of the total beta cell mass. Regarding the islets of Langerhans, it has been shown that about 75% of islets have multiple connections with ductal cells. The islet cell hormones have profound effects on exocrine pancreas function.[51]



Some researchers concluded that exocrine pancreatic disease is more common than previously believed in both diabetic and non-diabetic individuals, in agreement with autopsy studies that indicate pancreatic involvement in 13% of a "normal" population.[51]

e. Diabetes Type 3 and Chronic Pancreatitis

Hardt PD *et al.* (2008) [50] wrote in *Diabetes Care*, "Exocrine pancreatic insufficiency is frequently associated with diabetes, with high prevalence in both insulin-dependent (diabetes type 1) or insulin-independent (diabetes type 2) patients. Exocrine pancreatic failure has often been perceived as a complication of diabetes. In contrast, recent clinical observations lead to the notion that non-endocrine pancreatic disease is a critical factor for development rather than a sequel to diabetes. The incidence of diabetes caused by exocrine pancreatic disorders appears to be underestimated and may comprise 8% or more of the general diabetic patient population".

Some physicians refer to this condition as diabetes type 3.
Diabetes mellitus and exocrine function disorders of the pancreas have a close connection causing many gastrointestinal symptoms.[56]
In 2008, 30 international specialists were invited to the *Second Giessen International Workshop on Interactions of Exocrine and Endocrine Pancreatic Diseases* [51] to share their experience and thoughts covering the main topics of:
a) Pancreatic diabetes (type 3c)
b) Chronic inflammation of the pancreas

At the conference, it became accepted by most endocrinologists that exocrine dysfunction is frequent in diabetes mellitus. Concerning chronic pancreatitis, paradigms have started to evolve. Pancreatitis or pancreatic fibrosis appears to be frequent in Western societies and might affect more than 10% in population-based studies.

According to Hardt *et al*. [52] the digestive function in diabetes mellitus shows a high prevalence of pathological exocrine function in both type 1 and type 2 diabetic patients. Pancreatic insufficiency is very frequent in type 1 (about 50%) and type 2 diabetic patients (about 32%).

It is also possible that some of the diabetics are actually patients with chronic pancreatitis. However, chronic pancreatitis might be overlooked in clinical practice as symptoms of exocrine disease. These symptoms are not specific in the early stages of chronic pancreatitis. On the other hand, the prevalence of diabetes mellitus in chronic pancreatitis is 40-70%, and in chronic-calcifying pancreatitis up to 90%.[54]

There are also some interesting morphological findings in the exocrine pancreas in type 1 diabetes including

- Reduced weight of the pancreas
- Histological evidence of exocrine pancreas atrophy

In type 2 diabetes, the following was discovered:

- Reduced levels of fecal elastase in type 2 diabetes as compared to normal controls
- Severe exocrine pancreas impairment in 12% and moderate and severe impairment in 30% of patients
- Insufficiency more frequent in males even after correcting for strong alcohol consumption [55]

In 2001, Fransesco Marotta, MD, PhD from Milan, Italy, described an Italian study on chronic pancreatitis researched in 22 medical centers with regard to epidemiological, clinical, diagnostic, and therapeutic aspects. The study included 1,068 patients by the end of 2006. The mean age of the included patients was 52 years and 72% of the subjects were men. The age of disease onset was 45 for men and 42 for women. Only 61% of the diseased drank alcohol and of them, only 40% drank at least 80 g alcohol per day.

80% of the men and 45% of the women smoked. 1.5% of the patients had autoimmune pancreatitis and 1.2% had mutations of gene (CFTR). 27% of the patients had diabetes, but of the patients with autoimmune pancreatitis only 12% had diabetes. On the other hand, 59% had cholecystectomy (removal of gallbladders) and 18% had biliary stones. 12% of these patients had calcifications and 29% had steatorrhea.[51]

Pancreatic diabetes mellitus (DM) develops from the impairment of the pancreatic endocrine function due to the progression of a pancreatic disease such as pancreatitis, pancreatic surgery or pancreatic carcinoma. DM greatly affects the prognosis and quality of life in chronic pancreatitis:

it may lead to life-threatening complications such as severe hyperglycemia or to micro- and macro-angiopathic complications.

Czakó L *et al*. (2009) considered DM as an independent risk factor for mortality of patients with chronic pancreatitis (CP). [168] The incidence of pancreatic DM depends on several factors, such as the etiology and duration of CP, and the presence of pancreatic calcification. The endocrine functions are more disturbed in alcoholic CP than in nonalcoholic CP.[168]

The study by Ito T. *et al*. (2007) found that 67.8% of the patients with CP and newly diagnosed DM had an alcoholic etiology, and 34.3% of the patients with alcoholic CP developed DM over the 8-year follow-up period. Moreover, 43% of patients with newly developed DM were regular drinkers.[169]

The prevalence of chronic pancreatitis may be much higher in the general population than previously estimated and Diabetes Mellitus secondary to Chronic Pancreatitis could be more common, which would explain the frequent finding of exocrine pancreatic deficiency in diabetics.[50, 51, 52]

According to Hardt P.D. *et al.* (2008), "However, in light of the association between pancreas exocrine and endocrine deficiency, the concept of "shared injury" and common origin of exocrine and endocrine pancreatic precursor cells deserves greater attention".[50]

The authors strongly believe that this "shared injury" that can badly affect both exocrine and endocrine pancreatic function is **metabolic acidosis**. As we have mentioned already, in the base of many pancreatic disorders lies the acidifying of pancreatic juice and bile. Acidity both shuts down the sensitivity cells to insulin and negatively changes the biochemistry of bile and pancreatic juice. Acidity literally kills the pancreas!

Focus on acid – alkaline balance can be an important key to prevent and treat digestive and/or hormonal pancreatic disorders

f. Possible Role of Metabolic Acidosis in Development Metabolic Syndrome, Overweight, and Diabetes

There is evidence that acidity may be in the base of precursors of type 2 diabetes, such as obesity and Metabolic Syndrome.
This idea is not new. In 1963, a study conducted by Walker *et al*. "*Inhibition of Insulin by Acidosis*" proved that insulin did not work in acidic conditions.[44]

This study established a "golden rule" for intensive care doctors all over the world. In the treatment of patients with the diabetic ketoacidotic coma, doctors must ***"start to normalize the metabolic acidosis first and then normalize the level of blood glucose by using insulin."*** Otherwise insulin will not work. In the case of ketoacidosis, fats and proteins are metabolized

excessively and byproducts known as ketone bodies are produced. They are released into the bloodstream and cause decreased pH of the blood - severe metabolic acidosis.

In addition to insulin not working during acute metabolic acidosis, researchers revealed that chronic metabolic acidosis causes the insulin resistance (Metabolic Syndrome), as well.[45, 47, 48]

It is very likely that metabolic acidosis produces insulin resistance, which stimulates the programmed genetic response to starvation and food shortage. After that, the body will have to increasingly save every calorie consumed and store it as fat. Insulin resistance is closely connected to having excess weight and collection of fat especially in the belly. Insulin is a major anabolic hormone for glucose, lipid and protein metabolism.

The authors postulate that chronic metabolic acidosis is very common and may trigger the genetically programmed starvation mode of metabolism. One of the mechanisms of surviving of *Homo sapiens* is the lowering of metabolism due to famine. Humans do not have a large storage of carbohydrates, thus during scarcity of food, the body burns fat and muscle tissue protein for energy to survive. Burning fat and proteins causes severe acidosis and ketoacidosis. So, in case of chronic metabolic acidosis, even without starvation, blood pH changes may trigger the very complicated mechanism involving neuro-endocrine systems, the liver and the pancreas. It is known, the role of insulin, glucagon from the pancreas and cortisol from adrenal glands for regulating of the body weight.

Chronic metabolic acidosis may cause the imbalances in hepatic lipid metabolism, leading to the buildup of hepatic triglycerides and chronic inflammation. These processes are closely related to diseases such as obesity, diabetes, hyperlipidemia, atherosclerosis, fatty liver and fatty pancreas.

Chronic metabolic acidosis also contributes to a state of insulin resistance within the body by interfering with glucose delivery to the cells. Normally, ordinary levels of insulin will escort glucose into the cells. With acidosis, the cell receptors fail to recognize the insulin hormone and deny it access to deposit the glucose and cause sugar to build up within the bloodstream. The pancreas, unaware of the insulin resistance, increases insulin production in an effort to pump out enough of the hormone to heal the situation. The body interprets the lack of glucose within the cells as starvation and begins to convert every calorie into fat. As a result, obesity and diabetes ensue. Acidosis may be negatively involved in the insulin production by pancreatic beta cells, as well.

g. Metabolic Syndrome

Why is Metabolic Syndrome overspreading? Similar to other chronic diseases, Metabolic Syndrome is a complex, lifestyle induced illness, which is often triggered by metabolic acidosis. Normal adult humans eating modern-day diets have a chronic low-grade metabolic acidosis

whose severity is determined by the body's acid production and varies mainly with diet composition.[49]

Experts of the World Health Organization consider Metabolic Syndrome, Syndrome X or Insulin Resistance in people when they have 3 or more of the following symptoms:

> Excessive fat in and around the abdomen/abdominal or “central” obesity (“apple shape” and waist size of greater than 40 inches in men, greater than 35 inches in women)

> High levels of triglycerides (fats) above 150 mg/dl and LDL (bad) cholesterol in the blood

> Low levels of HDL (good) cholesterol less than 40 mg/dl (men) or under 50 mg/dl (women)

> High blood pressure (greater than 130/85)

> A fasting blood glucose (sugar) level greater than 110 mg/dl (6.1 mmol/L)

The Metabolic Syndrome is a cluster of risk factors associated with the development of cardiovascular disease and diabetes including obesity (in particular belly fat), insulin resistance and abnormal glucose metabolism coupled with high blood levels of cholesterol.

The authors are of the same opinion as Jun Seok Lee *et al.* who published in the article*, Clinical implications of fatty pancreas: Correlations between fatty pancreas and metabolic syndrome* (2009) that one of the important signs of Metabolic Syndrome aside from fatty liver is the fatty pancreas. Fatty pancreas was associated with higher levels of visceral fat, waist circumference, aspartate aminotransferase (AST), alanine aminotransferase (ALT), total cholesterol, triglycerides, high density lipoproteins, free fatty acids, g-GTP, insulin and the homeostasis model assessment of insulin resistance. Fatty pancreas also showed a strong correlation with Metabolic Syndrome and is an early marker of insulin resistance.[58]

Overweight persons with Metabolic Syndrome usually report GI complaints that are obviously connected with exocrine pancreatic deficiency disorders. Scientific data also confirms that insulin resistance may cause a reduction of pancreatic amylase content.[57]

A large body of epidemiological data correlates the presence of Metabolic Syndrome with an increased risk of cardiovascular disease, diabetes and overall mortality. Some physicians have coined Metabolic Syndrome as “a disease of our generation.” Some studies estimate the prevalence of Metabolic Syndrome in the United States to be up to 25% of the population.[334]

The latest published data from the Centers for Disease Control and Prevention, National Center for Health Statistics at the U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES, report that “approximately 34% of adults met the criteria for Metabolic Syndrome”.
www.cdc.gov/nchs/data/nhsr/nhsr013.pdf

It is well known that there are several connections between obesity, insulin resistance, Metabolic Syndrome and diabetes especially in the pancreatic diabetes. Decreased insulin sensitivity was demonstrated in pancreatic diabetes by the glucose-clamp method and insulin tolerance test [168].

We point out again that all these disorders are acidic conditions, which are caused by metabolic acidosis.

Additional evidence that chronic body acidity may play a role in developing these metabolic conditions is inner calcification. Chronic metabolic acidosis produces a negative calcium balance because of bone re-absorption and calcification of inner organs including the pancreas and blood vessels. A combination of osteoporosis and osteopenia with atherosclerosis is very common. Chronic pancreatitis usually is envisioned as an atrophic fibrotic gland with dilated ducts and calcifications.[15] The incidence of pancreatic diabetes depends on several factors such as the etiology and duration of chronic pancreatitis and the presence of pancreatic calcification.[168]

h. Endocrine function in different stages of exocrine pancreatic deficiency

It is the opinion of the authors that the disorders of exocrine and endocrine function develop simultaneously but the prevalence of symptoms can be different. *The Biotherapy Functional Clinical Classification of Exocrine Pancreatic Disorders* can be implemented to endocrine pancreatic disorders, as well.

The clinical experience of the authors shows that the beginning of the *acidic pancreas and bile* stage of exocrine pancreatic deficiency can often combine hypoglycemic situations with sugar craving, attacks of hunger, mood swings, and autonomic nervous system reactions.

Later in the advanced *pancreatic deficiency* stage, the diminished digestive function of the pancreas combines with Metabolic Syndrome. Low grade or severe metabolic acidosis is a major trigger of these maladies.

Because of acidic conditions, another mechanism that aggravates the gastro-intestinal disorders in patients with diabetes mellitus is bile salt malabsorption.[56] Acidic bile causes production of aggressive bile acids that decreases reabsorption of the bile derivates in the small intestine. Extra bile acids irritate the large intestine, causing loose stool or diarrhea in diabetic patients.

Overweight issues, obesity, high levels of blood triglycerides and possibly fatty pancreas and liver associate with Metabolic Syndrome and impair digestive pancreatic function.[58] All of these conditions have a close link to pancreatitis and possibly pancreatic cancer. Obesity is a definitive risk factor of severity and mortality in acute pancreatitis.[59]

The *pancreatic failure* stage is associated with the final stage of chronic pancreatitis and Pancreatic Insulin Depended Diabetes.

The Biotherapy Functional Clinical Classification of Exocrine Pancreatic Disorders may easily correlate problems of endocrine and exocrine pancreatic function and can help with choosing the healing actions in both digestive and metabolic problems.

1. *Acidic pancreas and bile* stage ==> ==> Hypoglycemic events

2. *Pancreatic Deficiency* stage ==> ==> Metabolic Syndrome, Diabetes - NIDDM

3. *Pancreatic failure* stage ==> ==> Pancreatic Insulin Depended Diabetes- IDDM

From 1998, when Stanford University professor Gerald Reaven, MD described Syndrome X, another name for Metabolic Syndrome, there have been a large number of medical articles and books published about this condition. Nevertheless, Metabolic Syndrome continues having many questions concerning its pathogenesis. The authors strongly believe that chronic metabolic acidosis, by blocking the sensitivity of human cells to insulin, is a main factor for the development of this "disease of our generation".

Later in this book, there is a healing program for all three stages of exocrine pancreatic deficiencies, including the correction of chronic metabolic acidosis and Metabolic Syndrome. Some of these healing methods are widely practiced in Europe and other continents.

Interesting facts at a glance:

The pancreas is a unique organ that performs multiple tasks with exocrine and endocrine function

Pancreatic cells produce digestive enzymes and bicarbonates that travel to the small intestine. This is the exocrine (digestive) pancreatic function. The pancreas is the main organ for digestion

Pancreatic cells produce hormones, which are released into the bloodstream. Insulin is a well-known hormone of the pancreas. This is the endocrine (hormonal) function. Pancreas is the major hormonal gland

The two pancreatic functions, digestive and hormonal, are interrelated and often have the same general reasons for malfunction

Diseases such as inflammation, infections, trauma, parasites, tumors, and hereditary and metabolic disorders of the pancreas negatively impact both digestive and hormonal functions

All functions of the pancreas, both digestive and hormonal, are dependent upon each other and are affected by nervous regulation, diet, lifestyle and toxic environments both inside and outside of the pancreas

In the United States, obesity, Metabolic Syndrome, diabetes, digestive disorders, IBS, dysbiosis, and a host of other similar diseases have been steadily rising until they have almost reached epidemic proportions

In almost all these conditions, exocrine and endocrine pancreatic function is diminished and may been observed signs of metabolic acidosis

The chronic metabolic acidosis negatively influences both the digestive and the hormonal functions of the pancreas

In periods of starvation, the body uses fat and muscle protein for energy to survive. Burning fat and protein produces many acidic substances that cause acidity in the body

Most individuals have a special genetic slow down metabolic mechanism to survive a period of starvation

Metabolic acidosis may trigger a possible starvation mode of slow metabolism

Current acid-causing diets deplete the body's alkaline reserve causing metabolic acidosis

During metabolic acidosis, insulin loses the responsibility to move glucose into the cells for energy. This condition is called insulin resistance and leads to Metabolic Syndrome

34% of Americans suffer from the Metabolic Syndrome that manifests with high blood pressure, belly fat obesity, fatty liver, fatty pancreas, and high levels of glucose, cholesterol, and triglycerides (fats) in the blood

If it is not properly treated, in 8-10 years, Metabolic Syndrome may lead to diabetes, heart attacks, strokes, dementia, etc.

Chronic metabolic acidosis produces a negative calcium balance as a result of bone re-absorption and the calcification of the inner organs, including the pancreas and blood vessels

A combination of osteoporosis, osteopenia with atherosclerosis and calcification of inner organs is very widespread

Calcification of the pancreas is a very common sign of chronic pancreatitis

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This is the end of the **Part I**: STRUCTURE, FUNCTION, AND DISORDERS OF THE PANCREAS of the e-book version of **HEALTHY PANCREAS, HEALTHY YOU**

Next parts are:

Part II: HEALING FOOD IN THE DIGESTIVE (PANCREATIC) AND METABOLIC DISORDERS

Part III: HOW TO IMPROVE THE EXOCRINE PANCREATIC FUNCTION, POSTPONE PANCREATIC DETERIORATION, AND HEAL DIGESTIVE (PANCREATIC) DISORDERS

References

These two interrelated parts focus on the healing diet, nondrug approaches for ***acidic pancreas and bile***, ***pancreatic deficiency***, and ***pancreatic failure*** stages of the exocrine pancreatic deficiency.

Contents of entire **HEALTHY PANCREAS, HEALTHY YOU** book can illustrate the topics of the other parts.

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About the Authors

Felix Melamed, LAc, MSTCM, CHt received a bachelor's degree in biology and psychology from Notre Dame de Namur University before pursuing a master's degree in Traditional Chinese Medicine from the Academy of Chinese Culture and Health Sciences in Oakland, CA.

He is currently in a private practice as an Executive Director of Biotherapy Alternative Medicine Clinic in San Francisco, California specializing in acupuncture, herbal medicine, clinical hypnosis, healing mineral water and detoxification modalities.

Mr. Felix Melamed is the author of a book "*Natural European Way of Whole Body Cleansing*" and many articles on diagnosis and nondrug treatment in Holistic and Traditional Chinese Medicine.

Felix Melamed is a composer and musician, author of 4 CDs of his songs and compositions. He is married and has a son. Information is available on his web site http://www.biotherapy-clinic.com/.

Peter Melamed, PhD received his medical education first as a registered nurse and then as a medical doctor in USSR. He took specialized training in anesthesiology, intensive care, and internal medicine. Working as a physician, he became interested in holistic healing through his

clinical experience with herbs, acupuncture, healing mineral water, and internal cleansing. He was granted a license to practice acupuncture in Russia in 1978, and from that time, he combined conventional Western medical treatment with herbs, acupuncture, and other nondrug healing therapies.

In 1975, Peter Melamed established Biotherapy as a natural, holistic approach to healing. Biotherapy combines the wisdom of traditional Russian folk medicine, ancient Oriental medical therapies, and European naturopathy with cutting-edge Western technology. He developed unique herbal remedies, acupuncture, magnet, cleansing, techniques, outpatient withdrawal from drugs and alcohol, drinking healing mineral water, etc.

After immigrating to the USA and passing CA and NCCAOM exams, Peter Melamed succeeded in starting up a private practice in 1996 at the Biotherapy Alternative Medicine Clinic of San Francisco Bay Area.

Peter Melamed, PhD is the author of a book "*Natural European Way of Whole Body Cleansing*" and many articles about nondrug treatment in English and Russian.

He is married and has three children and six grandchildren.
Information is available on his web site http://www.biotherapy-clinic.com/